

## FILING DETAILS:

PATENT NO	KIND	PATENT NO
DE 59205534	G Based on	EP 512403

PRIORITY APPLN. INFO: DE 1991-4115793 19910510

AB EP 512403 A UPAB: 19951109

The sensor array lies in the image plane of an optical system (2) perpendicular to the optical axis, with a microscanning system (9) with orthogonal translators (91, 92) indexing the sensor array relative to its initial position by a defined fraction of the mean spacing between the sensor elements.

Each of the measured image values has associated actual position values, with the microscanning synchronised via a sensor sequence control, using required position values dependent on the geometry of the sensor array.

USE - For vehicle quality control device or optical precision appts.

1/2

Dwg.1/2

FILE 'HOME' ENTERED AT 11:03:10 ON 13 NOV 2002

An INDEPENDENT CLAIM is also included for (1) for use in the novel device.

USE - For biological analysis, particularly denaturation, capture and then amplification of nucleic acid, optionally followed by hybridization testing of the amplicons (claimed).

ADVANTAGE - The device is relatively easy to make and very simple to use, since, once activated, the valves in the device require no external action to maintain them in position.

DESCRIPTION OF DRAWING(S) - The drawing shows a front view of an analysis card showing only the first level, for denaturing nucleic acid.

Entry port for sample 5

Sample entry channel 6

Entry valve 7

Sample separator 8

First transfer channel 9

Denaturing chamber 10

Drain 11

Bubble breaker 12

Buffer volume 15

Pin to support flexible film 16

Transfer line 17

Valve for transfer to second level 18

Thermal insulation 39

Entry for inert displacement fluid 61

Entry channel for inert fluid 62

Entry valve for inert fluid 63.

Dwg.2/5

L99 ANSWER 42 OF 42 WPIDS (C) 2002 THOMSON DERWENT

ACCESSION NUMBER: 1992-374731 [46] WPIDS

DOC. NO. NON-CPI: N1992-285642

TITLE: Precision video grammetric measuring system using two-dimensional sensor array - uses micro-scanning system to index latter by fraction of mean sensor spacing.

DERWENT CLASS: S02 W04 X25

INVENTOR(S): GITTLER, G; KUEHNERT, J; MOORE, T; RICHTER, U

PATENT ASSIGNEE(S): (RHEM) RHEINMETALL JENOPTIK OPTICAL METROLOGY; (ZEIS) JENOPTIK JENA GMBH; (RHEM) RHEINMETALL JENOPTIK OPTIC METROLOGY GMBH

COUNTRY COUNT: 6

PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
EP 512403	A2	19921111	(199246)*	GE	7
R: AT CH DE FR GB LI					
DE 4115793	A	19921112	(199247)		5
DE 4115793	C2	19930930	(199339)		5
EP 512403	A3	19930609	(199404)		
EP 512403	B1	19960306	(199614)	GE	10
R: AT CH DE FR GB LI					
DE 59205534	G	19960411	(199620)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
EP 512403	A2	EP 1992-107344	19920429
DE 4115793	A	DE 1991-4115793	19910510
DE 4115793	C2	DE 1991-4115793	19910510
EP 512403	B1	EP 1992-107344	19920429
DE 59205534	G	DE 1992-505534	19920429
		EP 1992-107344	19920429

L99 ANSWER 41 OF 42 WPIDS (C) 2002 THOMSON DERWENT  
 ACCESSION NUMBER: 2001-091506 [10] WPIDS  
 DOC. NO. CPI: C2001-026992  
 TITLE: Device for biological analysis e.g. nucleic acid  
 amplification using analysis cards, comprises elements  
 integral to the card to control the reaction sequence and  
 fluid transfers.  
 DERWENT CLASS: B04 D16 J04  
 INVENTOR(S): COLIN, B; DACHAUD, J; JARAVEL, C; PRIVAT, M T; PARIS, C;  
 PRIVAT, M  
 PATENT ASSIGNEE(S): (INMR) BIOMERIEUX SA  
 COUNTRY COUNT: 95  
 PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2000078452	A1	20001228	(200110)*	FR	34
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TZ UG ZW W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW					
FR 2795518	A1	20001229	(200110)		
AU 2000064508	A	20010109	(200122)		
EP 1187678	A1	20020320	(200227)	FR	
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL RO SI					

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2000078452	A1	WO 2000-FR1718	20000621
FR 2795518	A1	FR 1999-8117	19990622
AU 2000064508	A	AU 2000-64508	20000621
EP 1187678	A1	EP 2000-951631	20000621
		WO 2000-FR1718	20000621

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 2000064508	A Based on	WO 200078452
EP 1187678	A1 Based on	WO 200078452

PRIORITY APPLN. INFO: FR 1999-8117 19990622

AB WO 200078452 A UPAB: 20010220

NOVELTY - A device (A) using an analysis card (1), where the reaction sequences and transfers of fluid are controlled by elements within (1), is new. (1) comprises at least two reaction pathways, in parallel, and (A) includes at least one activator for each pathway. The device includes a system for advancing the card relative to the activator and/or advancing the activator relative to the card.

DETAILED DESCRIPTION - A device (A) using an analysis card (1), where the reaction sequences and transfers of fluid are controlled by elements within (1), is new. (1) comprises at least two reaction pathways, in parallel, and (A) includes at least one activator for each pathway. The device includes a system for advancing the card relative to the activator and/or advancing the activator relative to the card. All activators are at a constant, preferably identical, distance from each other and each pathway includes at least two fluid transfers, in series.

mixtures easier, faster and more accurate.  
Dwg.0/16

L99 ANSWER 40 OF 42 WPIDS (C) 2002 THOMSON DERWENT  
ACCESSION NUMBER: 2001-147207 [15] WPIDS  
DOC. NO. NON-CPI: N2001-107788  
DOC. NO. CPI: C2001-043547  
TITLE: System for analyzing data from a scatter plot of a  
**microarray biochip** for characterizing  
cancer cells comprises a device for producing and  
displaying scatter plots and a device for determining  
boundaries for data by selection criteria.  
DERWENT CLASS: B04 D16 S03  
INVENTOR(S): SCHERMER, M J; STEPHAN, T J  
PATENT ASSIGNEE(S): (GSIL-N) GSI LUMONICS INC  
COUNTRY COUNT: 20  
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2001004603	A1	20010118	(200115)*	EN	24
RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE					
W: CA JP					

## APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2001004603	A1	WO 2000-US18036	20000629

PRIORITY APPLN. INFO: US 1999-349334 19990708

AB WO 200104603 A UPAB: 20010317

NOVELTY - A scanner system for analyzing data comprises:

(1) a device (A) for producing and displaying a scatter plot  
containing a plotted point for each of the data; and

(2) a boundary device (B) for determining boundaries for segmenting  
the data based on specified selection data and displaying the boundaries  
in the scatter plot.

USE - The system is used for analyzing data from scatter plots  
containing outlier points far from the identity line produced from a  
fluorescent nucleic acid assay of cancerous and normal cells, produced  
from **microarray biochips**, by determining the  
boundaries for the segmenting data according to the selection criteria,  
and genetically characterizes the cancerous cells.

ADVANTAGE - The system analyzes a scatter plot containing hundred or  
thousands of data points, whose expression ratio is difficult to determine  
in prior art methods and also the points which are just above or just  
below any particular expression level threshold. The system also analyzes  
the data based on absolute expression level, or combines the several  
criteria or interactively specifies various selection criteria. The system  
may be used to analyze data from any type of scatter plot and designate  
the outlier points in the scatter plot, in addition to analyzing  
differential gene expressions.

DESCRIPTION OF DRAWING(S) - The figure shows the functional block  
diagram of the system.

scatter plot processor 12

fluorescent reader 14

dots 16

**microarray** 18

display 20

keyboard 22

Dwg.1/6

analyte receptor complex; and

(b) detecting a spectral feature associated with the analyte receptor complex;

(10) a method for manufacturing a particle structure, comprising:

(a) providing particles;

(b) linking the particles with first chemical linkers having a first linker length, forming first tier particle structures; and

(c) linking the first tier particle structures with second chemical linkers having a second linker length, forming second tier particle structures having resonance domains;

(11) method for manufacturing a chemically linked particle structure comprising:

(a) providing a first and second pool of particles;

(b) providing first nucleic acid linkers each with a proximal end with a linking group and a distal end with a nucleotide sequence with a first length;

(c) attaching 2 of the first nucleic acid linkers to particles of the first pool;

(d) providing second nucleic acid linkers each with a proximal end with a linking group and a distal end with a nucleotide sequence complementary to at least a portion of the sequence of the distal end of the first nucleic acid linker, where the orientation of the complementary **strand** is antiparallel;

(e) attaching 2 second nucleotide linkers to a substantial number of each particle of the second pool;

(f) mixing the first and second pool of particles together, permitting the complementary particles of the first and second nucleotide linkers to associate with each other;

(g) covalently linking complementary nucleic acid sequences together forming pairs of particles;

(h) dividing the pool of particle pairs into third and fourth pools;

(i) providing third nucleic acid linkers each with a proximal end with a linking group and a distal end with a nucleotide sequence of a third length;

(j) attaching about 2 of the third nucleic acid linkers to a substantial number of particle pairs of the third pool;

(k) providing fourth nucleic acid linkers each with a proximal end with a linking group and a distal end with a nucleotide sequence complementary to at least a portion of the sequence of the distal end of the third nucleic acid chemical linker, where the orientation of the complementary strand is antiparallel;

(l) attaching about 2 fourth nucleotide linkers to a substantial number of each nanoparticle pairs of the fourth pool;

(m) mixing the third and fourth pool of particles together, permitting the complementary particles of the third and fourth nucleotide linkers to associate with each other; and

(n) covalently linking complementary third and fourth nucleic acid sequences together;

(12) a Raman reader comprising a light source, a matrix array with particle structures, a holder for positioning the matrix array in relation to the light source and a light detector; and

(13) method for detecting an analyte on a biochip comprising providing a biochip with at least one defined area with at least one analyte receptor and one identifier, providing a Raman reader, exposing the biochip to a solution containing an analyte, allowing analyte receptor complexes to form, exposing the defined area to incident light, collecting light emitted from a defined area and determining the position of the defined area.

USE - The particles enhance the signal during analyte detection in connection with Raman spectroscopy. The particles are especially suitable for the detection of nucleic acids or other biological molecules in the diagnosis of disease.

ADVANTAGE - The particles make the detection of analytes in complex

NL OA PT SD SE SL SZ TZ UG ZW  
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DZ  
EE ES FI GB GD GE GH GM HU ID IL IN IS JP KE KG KP KR KZ LC LK LR  
LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI  
SK SL TJ TM TR TT TZ UA UG UZ VN YU ZA ZW  
AU 2000077165 A 20010430 (200142)  
US 2001053521 A1 20011220 (200206)  
EP 1242510 A1 20020925 (200271) EN  
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT  
RO SE SI

## APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2001023459	A1	WO 2000-US26386	20000926
AU 2000077165	A	AU 2000-77165	20000926
US 2001053521	A1 Provisional	US 1999-156195P	19990927
	CIP of	US 2000-670453	20000926
		US 2001-815909	20010323
EP 1242510	A1	EP 2000-966884	20000926
		WO 2000-US26386	20000926

## FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 2000077165	A Based on	WO 200123459
EP 1242510	A1 Based on	WO 200123459

PRIORITY APPLN. INFO: US 1999-156471P 19990927; US 1999-156145P  
19990927; US 1999-156195P 19990927; US  
2000-670453 20000926; US 2001-815909 20010323

AB WO 200123459 A UPAB: 20021105

NOVELTY - Particles structures with receptors are used in analyte detection using Raman spectroscopy.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for:

- (1) particle structure (A) comprising a fractal structure and a receptor;
- (2) a particle structure (B) comprising at least 1 resonance domain and an analyte receptor near the resonance domain;
- (3) a particle structure (C) comprising particles with resonance domains and analyte receptors preferentially bound near the resonance domains;
- (4) particle structures for binding an analyte comprising at least one resonance domain and an analyte receptor that is devoid of at least one Raman spectroscopic feature of the analyte;
- (5) a suspension of fractal associates comprising a liquid and fractal associates;
- (6) a surface with fractal associates;
- (7) a **biochip** comprising:
  - (a) a substrate;
  - (b) (C); and
  - (c) a defined area with analyte receptors preferentially localized near the resonance domains;
- (8) a system for analyte detection, comprising:
  - (a) a substrate with defined areas with different (C), having preferential analyte binding affinity different from the binding affinities of analyte receptors associated with different defined areas;
  - (b) identifiers for each of the different areas; and
  - (c) a detector associated with a defined area on the substrate;
- (9) a method for analyte detection, comprising:
  - (a) exposing the analyte to the receptor on the particles to form an

comprising at least 1 character string corresponding to the polyNt (I), or to a polyP encoded by the polyNt;

(13) a method (XIII) of identifying a seq similar or homologous to at least 1 of the polyNt (I) or at least 1 of the polyPs encoded by the polyNt, comprising:

(a) providing a seq database; and

(b) querying the seq database with at least 1 target seqs corresponding to the polyNts or to the polyPs to identify at least 1 seq members of the database that display seq similarity or homology to at least 1 of the target seqs;

(14) a plant (XIV) comprising altered expression levels of (I) and/or (VII); and

(15) a plant (XV) lacking a Nt seq encoding (VII).

ACTIVITY - Pesticidal; antimicrobial.

No relevant/quantitative biological data given.

MECHANISM OF ACTION - Gene therapy.

USE - The polynucleotides (I) and the polypeptides (VII) they encode may be used to alter the structure and developmental characteristics of plants such as soybean, wheat, corn, potato, cotton, rice, oilseed rape, sunflower, alfalfa, sugar cane, turf, banana, blackberry, blueberry, strawberry, raspberry, cantaloupe, carrot, cauliflower, coffee, cucumber, eggplant, grapes, honey dew, lettuce, mango, melon, onion, papaya, peas, peppers, pineapple, spinach, squash, sweet corn, tobacco, tomato, watermelon, rosaceous fruits and/or vegetable brassicas (claimed).

Specifically, they are used for modifying traits associated with a plant's pathogen tolerance such as alterations in cell wall composition, trichome number or structure, callose induction, phytoalexin induction and/or alterations in the cell death response. Transgenic plants expressing (I) or (VII) are more tolerant to biotrophic or necrotrophic pathogens such as fungi, bacteria, mollicutes, viruses, nematodes and parasitic higher plants.

ADVANTAGE - Transcription factors are key controlling elements of biological pathways and altering expression levels of 1 or more transcription factors can change entire biological pathways in an organism. For example, manipulation of the levels of selected transcription factors may result in increased expression of economically useful proteins or metabolic chemicals in plants or to improve other agriculturally relevant characteristics. Conversely, blocked or reduced expression of a transcription factor may reduce biosynthesis of unwanted compounds or remove an undesirable trait. Therefore manipulating transcription factor levels in plants offers great potential in agricultural biotechnology for modifying a plant's traits.

Dwg.0/3

L99 ANSWER 39 OF 42 WPIDS (C) 2002 THOMSON DERWENT  
ACCESSION NUMBER: 2001-328180 [34] WPIDS  
CROSS REFERENCE: 2001-273523 [28]; 2002-113919 [15]  
DOC. NO. CPI: C2001-100656  
TITLE: Particles structures with receptors are used in analyte detection using Raman spectroscopy for the detection of nucleic acids or other biological molecules in the diagnosis of disease.  
DERWENT CLASS: A89 B04 D16  
INVENTOR(S): KREIMER, D I; NUFERT, T H; YEVIN, O A; NUFERT, T F  
PATENT ASSIGNEE(S): (ARRA-N) ARRAY BIOSCIENCE CORP; (KREI-I) KREIMER D I; (NUFE-I) NUFERT T H; (YEVI-I) YEVIN O A  
COUNTRY COUNT: 93  
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
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WO 2001023459	A1	20010405	(200134)*	EN	88
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RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ

AB WO 200135726 A UPAB: 20020924

NOVELTY - Polynucleotides (I) encoding 29 plant transcription factor polypeptides (VII) which may be used to modify traits associated with a plant's pathogen and pest resistance characteristics when their expression level is altered, are new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are included for the following:

(1) an isolated or recombinant polynucleotide (polyNt) (I) comprising a nucleotide (Nt) sequence (seq) selected from:

(a) a Nt seq encoding a polypeptide (polyP) comprising 1 of 29 defined amino acid (aa) seqs ((A1)-(A29)) given in the specification, or a complementary nucleic acid (NA) seq;

(b) a Nt seq encoding a polyP comprising a conservatively substituted variant of the polyP of (a);

(c) a Nt seq comprising a seq selected from 29 defined Nt seqs ((N1)-(N29)) given in the specification, or a complementary NA seq;

(d) a Nt seq comprising silent substitutions in a Nt of (c);

(e) a Nt seq which hybridizes under stringent conditions to a Nt seq of (a)-(d);

(f) a Nt seq comprising at least 15 consecutive Nts of a seq of (a)-(e);

(g) a Nt seq comprising a subsequence (s-seq) or fragment of (a)-(f), which encodes a polyP that modifies a plant's structure and/or developmental characteristics;

(h) a Nt seq having at least 31% identity (id) to a Nt seq of (a)-(g);

(i) a Nt seq having at least 60% id to a Nt seq of (a)-(g);

(j) a Nt seq which encodes a polyP having at least 31% id to a polyP of (A1)-(A29);

(k) a Nt seq which encodes a polyP having at least 60% id to a polyP of (A1)-(A29); and/or

(l) a Nt seq which encodes a conserved domain of a polyP having at least 65% seq id to a conserved domain of a polyP of (A1)-(A29);

(2) a cloning or expression vector (II) comprising (I);

(3) a cell (III) comprising (II);

(4) a transgenic plant (IV) with a modified structure and developmental characteristics, which comprises the recombinant polyNt (I);

(5) a composition (V) produced by incubating at least 1 of the polyNts (I) with a nuclease, a restriction enzyme, a polymerase, a polymerase and a primer, a cloning vector and/or a cell;

(6) a composition (VI) comprising at least 2 of the polyNts (I);

(7) an isolated or recombinant polyP (VII) comprising a s-seq of at least 15 contiguous aa encoded by the recombinant or isolated polyNt (I);

(8) a plant (VIII) which ectopically expresses the isolated polyP (VII);

(9) a method (IX) for producing a plant having modified structure and developmental characteristics, comprising altering the expression of (I) or the expression levels or activity of (VII) in a plant to produce a modified plant and selecting the plant for those modified characteristics;

(10) a method (X) of identifying a factor that is modulated by, or interacts with a polyP encoded by the polyNt (I), comprising:

(a) expressing a polyP encoded by the polyNt in a plant; and

(b) identifying at least 1 factor that is modulated by or interacts with the polyP;

(11) a method (XI) of identifying a molecule that modulates activity or expression of a polyNt or polyP of interest, comprising:

(a) placing the molecule in contact with a plant comprising the polyNt or the polyP encoded by (I); and monitoring:

(i) expression level of the polyNt in the plant;

(ii) expression level of the polyP in the plant;

(iii) modulation of an activity of the polyP in the plant; and/or

(iv) modulation of an activity of the polyNt in the plant;

(12) an integrated system, computer or computer readable medium (XII)



(23) a kit for joining, deleting, or replacing nucleic acid segments.  
USE - The method is useful for producing a population of hybrid nucleic acids which may be the same or different. The nucleic acids may be used to express therapeutic proteins or peptides and they may also be used to create novel fusion proteins by expressing different sequences linked to each other.

ADVANTAGE - The method allows simultaneous cloning of two or more different nucleic acids.

Dwg.0/27

L99 ANSWER 38 OF 42 WPIDS (C) 2002 THOMSON DERWENT  
ACCESSION NUMBER: 2001-335978 [35] WPIDS  
CROSS REFERENCE: 2001-266398 [27]; 2001-335977 [35]; 2001-335979 [35];  
2001-335996 [35]; 2001-335999 [35]; 2001-336000 [35];  
2002-292022 [33]  
DOC. NO. NON-CPI: N2001-242506  
DOC. NO. CPI: C2001-103872  
TITLE: Nucleic acids encoding plant transcription factor  
polypeptides, useful for altering the pathogen resistance  
characteristics of plants, e.g. corn, potato and cotton  
plants.  
DERWENT CLASS: C06 D16 P13  
INVENTOR(S): ADAM, L; CREELMAN, R; HEARD, J; JIANG, C; PINEDA, O;  
RATCLIFFE, O; REUBER, L  
PATENT ASSIGNEE(S): (ADAM-I) ADAM L; (CREE-I) CREELMAN R; (HEAR-I) HEARD J;  
(JIAN-I) JIANG C; (MEND-N) MENDEL BIOTECHNOLOGY INC;  
(PINE-I) PINEDA O; (RATC-I) RATCLIFFE O; (REUB-I) REUBER  
L  
COUNTRY COUNT: 95  
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2001035726	A1	20010525	(200135)*	EN	130
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW					
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW					
AU 2001019199	A	20010530	(200152)		
EP 1229782	A1	20020814	(200261)	EN	
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI TR					

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2001035726	A1	WO 2000-US31418	20001114
AU 2001019199	A	AU 2001-19199	20001114
EP 1229782	A1	EP 2000-982129	20001114
		WO 2000-US31418	20001114

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 2001019199	A Based on	WO 200135726
EP 1229782	A1 Based on	WO 200135726

PRIORITY APPLN. INFO: US 2000-227439P 20000822; US 1999-166228P  
19991117; US 2000-197899P 20000417

19991210; US 2000-732914 20001211

AB WO 200142509 A UPAB: 20020903

NOVELTY - A new method (M1) of producing a population of hybrid nucleic acids (HNA) comprises mixing at least a first population of nucleic acids (F1) comprising one or more recombination sites with at least one target nucleic acid comprising one or more recombination sites and causing some or all of F1 to recombine with all or some of the target nucleic acids.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) a method (M2) of producing HNA comprising F1 with at least a second population of nucleic acid molecules comprising one or more recombination sites and causing some or all F1 to recombine with all or some nucleic acid molecules of the second population;

(2) a method (M3) for performing homologous recombination between nucleic acid molecules

(3) a method (M4) for targeting or mutating a target gene or nucleotide sequence;

(4) a recombinant host cell produced by M4;

(5) a method (M5) of cloning a nucleic acid molecule;

(6) a method (M6) of cloning 'n' nucleic acid segments, where n is an integer greater than 1 or 2;

(7) a nucleic acid molecule produced by M5;

(8) a method (M7) of joining two segments of nucleic acid;

(9) a method (M8) of joining 'n' nucleic acid segments, where 'n' is an integer greater than 2;

(10) a composition comprising the HNA produced by M1 or the joined nucleic acid segments prepared by M7 or M8;

(11) a population of recombinant host cells comprising HNA produced by M1 or the joined nucleic acid segments prepared by M7 or M8;

(12) a method of making a population of recombinant host cells comprising introducing HNA produced by M1 or the joined nucleic acid segments prepared by M7 or M8 into a host cell;

(13) a method (M9) of altering properties of a cell comprising introducing into the cell nucleic acid segments joined by M8;

(14) a method (M10) of synthesizing a protein comprising providing a nucleic acid molecule comprising a coding sequence followed by a stop codon, where the nucleic acid molecule is flanked by at least one recombination site, providing a vector comprising at least one recombination site and a coding sequence, causing recombination such that the nucleic acid molecule is inserted into the vector to produce a modified vector with the two coding sequences connected in frame, transforming a host cell which expresses a suppressor tRNA with the modified vector and causing expression of the two coding sequences such that a fusion protein encoded by at least a portion of both of the coding sequences is produced, where either the nucleic acid molecule or the vector comprises at least one suppressible stop codon;

(15) a method (M11) for determining the gene expression profile in a cell or tissue;

(16) a method (M12) for preparing and identifying a nucleic acid molecule containing two or more nucleic acid segments which encode gene products involved in the same biological process or biological pathway;

(17) a nucleic acid molecule produced by M12;

(18) a support comprising at least one first nucleic acid molecule, where the first nucleic acid molecule comprises one or more recombination sites or its portions;

(19) a composition comprising the above support and at least one second nucleic acid molecule or protein or peptide molecule having at least one recombination site or its portion;

(20) a method (M13) for attaching or binding one or more nucleic acid molecules, protein or peptide molecules, or other compounds to a support;

(21) a solid or semisolid support prepared by M13;

(22) a method (M14) for linking or connecting two or more molecules or compounds of interest; and

identifying cancer prognostic markers, assessing or choosing a therapy, or finding a biochemical therapy target, preferably in tumors (all claimed).

ADVANTAGE - The apparatus works at high speed and is automated.

DESCRIPTION OF DRAWING(S) - The drawing shows a system for automated, high-speed fabrication of tissue microarrays, showing a storage station for tissue blocks.

specimen source 102  
retriever 104  
detector 105  
constructor 106  
sectioner 108  
reagent station 110  
scanner 112  
controller 114  
digital camera 160  
Dwg.1/29

L99 ANSWER 37 OF 42 WPIDS (C) 2002 THOMSON DERWENT

ACCESSION NUMBER: 2001-356174 [37] WPIDS

CROSS REFERENCE: 2002-519662 [55]

DOC. NO. CPI: C2001-110519

TITLE: Producing hybrid nucleic acids, useful for expressing novel therapeutic polypeptides, by mixing the same or different nucleic acids having one or more recombination sites in the presence of recombination proteins, e.g. Cre.

DERWENT CLASS: B04 D16

INVENTOR(S): BRASCH, M A; BYRD, D R N; CHEO, D; HARTLEY, J L; TEMPLE, G F

PATENT ASSIGNEE(S): (BRAS-I) BRASCH M A; (BYRD-I) BYRD D R N; (CHEO-I) CHEO D; (HART-I) HARTLEY J L; (TEMP-I) TEMPLE G F

COUNTRY COUNT: 94

PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2001042509	A1	20010614	(200137)*	EN	358
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW					
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG UZ VN YU ZA ZW					
AU 2001020851	A	20010618	(200161)		
US 2002007051	A1	20020117	(200212)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2001042509	A1	WO 2000-US33546	20001211
AU 2001020851	A	AU 2001-20851	20001211
US 2002007051	A1	Provisional	US 1999-169983P 19991210
		Provisional	US 2000-188020P 20000309
			US 2000-732914 20001211

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 2001020851	A Based on	WO 200142509

PRIORITY APPLN. INFO: US 2000-188020P 20000309; US 1999-169983P

(d) a processor;  
    (e) an image analyzer imaging microarray sections; and  
    (f) a database storing tissue identifying information and information obtained from analysis of sections;  
    (8) examining (M4) a sample comprising:  
        (a) providing samples in an array;  
        (b) analyzing the samples; and  
        (c) examining to detect a marker;  
    (9) examining (M5) samples comprising:  
        (a) placing elongated samples at identifiable positions in a substrate;  
        (b) sectioning the substrate to provide copies of an array of the samples;  
        (c) disseminating one or more copy to others; and  
        (d) comparing an interpretation of one or more copy to an interpretation of one or more reference copy;  
    (10) making (M6) a library of tissue specimens comprising:  
        (a) placing elongated samples in a substrate; and  
        (b) sectioning the substrate to provide copies of an array of the samples;  
    (11) reviewing (M7) specimens comprising:  
        (a) providing sections comprising samples;  
        (b) obtaining images of sections after exposing the sections to reagents; and  
        (c) disseminating the images to recipients;  
    (12) standardizing (M8) pathological evaluations comprising:  
        (a) visualizing a specimen in a cross-section of a microarray of specimens, where the array comprises specimens in a 2D microarray;  
        (b) evaluating a biological characteristic of the specimen; and  
        (c) comparing the evaluation to a standard;  
    (13) training (M9) a person in histological analysis comprising providing a section of a microarray as in M8 (a) and tissue-specific information for a specimen in the array, and comparing the evaluation of the person with information for the specimen;  
    (14) parallel tissue evaluation (M10) comprising:  
        (a) displaying a computer generated image of a specimen in a microarray;  
        (b) producing an image evaluation for a clinical parameter; and  
        (c) comparing the evaluation to a reference; and  
    (15) parallel evaluation (M11) of a cross-section of a cellular specimen comprising:  
        (a) visualizing a cross-section of the specimen in a microarray as in M8 (a), where an immunological analysis, histological stain or nucleic acid hybridization has been performed on each specimen;  
        (b) analyzing a cross-section by examining the results of (a) to evaluate a clinical parameter; and  
        (c) comparing the evaluation to a standard evaluation of each of the specimens; or  
        (d) (a), where the specimens have been produced in one place;  
        (e) analyzing the first cross-section by examining the results of (d) in the first specimen to evaluate a clinical parameter for one specimen; and  
        (f) visualizing a second cross-section of a second specimen in a microarray as in (d), where the specimen has been produced in another place;  
        (g) analyzing the second cross-section of the specimen by examining the results of (f) to evaluate a clinical parameter for the second specimen; and  
        (h) comparing the evaluations to compare the biological analyses.  
USE - (I) is used to assemble tissue microarrays (claimed). (III) and M2 are used to detect a mutation in the sample (claimed). M4 is used to perform quality control and to compare reagent performance (claimed). M7 is used to evaluate a reagent for disease diagnosis or treatment,

AB WO 200142796 A UPAB: 20021018

NOVELTY - An apparatus (I) for assembling tissue arrays comprises:

- (i) a donor specimen compartmentalized station (Ia);
- (ii) a computer readable specimen identifier (Ib);
- (iii) a donor block scanner (Ic);
- (iv) a tissue array fabricator (Id);
- (v) a sectioner (Ie);
- (vi) a processing station (If) sections to different biological markers that associate with substrates in the sections; and
- (vii) a scanner (Ig).

DETAILED DESCRIPTION - (Ic) determines the specimen location in the carrier; (Id) obtains elongated specimen samples and places them in a recipient block; (Ie) sections the recipient block; (If) exposes sections to different biological markers; and (Ig) detects the presence of the biomarkers.

INDEPENDENT CLAIMS are also included for the following:

- (1) an automated apparatus (II) for preparing tissue specimens comprising:
  - (a) a specimen source (IIa);
  - (b) a retriever (IIb);
  - (c) a constructor (IIc) that removes samples from specimens and arrays them in three dimensional (3D) arrays in substrates, where some of the places correspond to samples from different specimens; and
  - (d) a controller (IId) directing the retriever and constructor;
- (2) an apparatus (III) for constructing tissue arrays from specimens comprising:
  - (a) a donor source (IIIa);
  - (b) (IIb);
  - (c) (IIc); and
  - (d) (IId) which identifies samples within the array;
- (3) an automated device (IV) for performing analysis of biological specimens comprising:
  - (a) means (IVa) for storing specimens embedded in medium;
  - (b) (I);
  - (c) means (IVb) for reacting the corresponding sections of the recipient substrates with reagents;
  - (d) means for detecting a presence and/or quantity of reagent in the sections; and
  - (e) computer for recording subject information and correlating it with presence and/or quantity of reagent;
- (4) performing (M1) analysis of specimens comprising:
  - (a) providing sections comprising samples;
  - (b) exposing the sections to reagents;
  - (c) obtaining images of the sections; and
  - (d) analyzing the images to determine if a reaction has occurred;
- (5) performing (M2) analysis of specimens comprising:
  - (a) obtaining samples from one or more sample using (I); and
  - (b) performing one or more cell free analysis to observe marker(s);
- (6) constructing (M3) tissue microarrays from donor specimens comprising:
  - (a) providing an array of blocks, each including a specimen embedded in medium and identifiable in an array;
  - (b) retrieving identified blocks from the array;
  - (c) obtaining samples from the blocks and inserting samples from the specimen into blocks; and
  - (d) sectioning the blocks;
- (7) a computer implemented system (V) for rapid construction and analysis of tissue microarray sections comprising:
  - (a) a retriever obtaining recipient blocks from a block array and transferring them to a sectioner;
  - (b) the sectioner cutting sections from blocks for mounting on a solid support;
  - (c) a conveyer;

, pharmaceuticals, dyestuffs, synthetic receptors or receptor ligands, and the like.

ADVANTAGE - The system gives a high local resolution, and the non-specific background illumination is eliminated, especially in the evaluation of **bio-chips**.

DESCRIPTION OF DRAWING(S) - The drawing shows a schematic layout for a fluorescence scanner.

fluorescence scanner 10  
pulsed laser 11  
excitation light beam 12  
**bio-chip** 15  
detector 25  
control computer 30  
Dwg.1/11

L99 ANSWER 36 OF 42 WPIDS (C) 2002 THOMSON DERWENT  
ACCESSION NUMBER: 2001-390062 [41] WPIDS  
CROSS REFERENCE: 2002-547861 [58]  
DOC. NO. NON-CPI: N2001-286963  
DOC. NO. CPI: C2001-118888  
TITLE: Apparatus used for assembly of tissue arrays comprises multicomponent parts e.g. array fabricator, sectioner, processing station.  
DERWENT CLASS: B04 D16 S03  
INVENTOR(S): KAKAREKA, J W; KALLIONIEMI, O; KONONEN, J; LEIGHTON, S B; POHIDA, T J; SALEM, G H; SAUTER, G  
PATENT ASSIGNEE(S): (USSH) US DEPT HEALTH & HUMAN SERVICES; (USSH) US NAT INST OF HEALTH  
COUNTRY COUNT: 95  
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
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WO 2001042796	A1	20010614	(200141)*	EN	136
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW					
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW					
AU 2001024329	A	20010618	(200161)		
EP 1238286	A1	20020911	(200267)	EN	
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL RO SI					

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
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WO 2001042796	A1	WO 2000-US34043	20001213
AU 2001024329	A	AU 2001-24329	20001213
EP 1238286	A1	EP 2000-988081	20001213
		WO 2000-US34043	20001213

FILING DETAILS:

PATENT NO	KIND	PATENT NO
-----		
AU 2001024329	A Based on	WO 200142796
EP 1238286	A1 Based on	WO 200142796

PRIORITY APPLN. INFO: US 1999-171262P 19991215; US 1999-170461P  
19991213

L99 ANSWER 35 OF 42 WPIDS (C) 2002 THOMSON DERWENT  
 ACCESSION NUMBER: 2002-218030 [28] WPIDS  
 DOC. NO. NON-CPI: N2002-167091  
 DOC. NO. CPI: C2002-066939  
 TITLE: Registering the presence of immobilized substances on a  
**bio-chip** carrier, comprises using a  
 fluorescence scanner, where a pulsed laser excites  
 fluorescent markings to be detected between the pulses  
 with local resolution.  
 DERWENT CLASS: B04 C07 D16 S03  
 INVENTOR(S): GRILL, H; LECLERC, N; PRIX, L; SCHUETZ, A  
 PATENT ASSIGNEE(S): (GIES-I) GIESING M; (MICR-N) SL MICROTEST WISS GERAETE  
 GMBH  
 COUNTRY COUNT: 1  
 PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
DE 10038080	A1	20020221	(200228)*		15

# APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
DE 10038080	A1	DE 2000-10038080	20000804

PRIORITY APPLN. INFO: DE 2000-10038080 20000804

AB DE 10038080 A UPAB: 20020502

NOVELTY - To show the presence of immobilized substances on a carrier, a series of light pulses are directed at the defined surface under study as an excitation light beam, fluorescent light is detected between successive light pulses, shown by the substances in the measurement field, and the light beams and the carrier are moved in relation to each other until a sufficient surface area has been scanned.

DETAILED DESCRIPTION - To register the presence of immobilized substances on a carrier, fluorescent light is detected by time resolution by a time-correlated count of the separate photons. The fluorescent light is detected by a confocal action where the excitation light is focused on to the carrier surface, or by wavelength-related means. The measurement field defined by the excitation light on the carrier has a diameter of 1 - 20 micro m full width half maximum (FWHM). The carrier supports the immobilized substances in a two-dimensional pattern. The light beam and the carrier are moved in relation to each other so that the elements of the two-dimensional pattern are given a sequential scanning. The carrier surface is scanned by deflection of the excitation light beam and by sliding the carrier on a plane parallel to its surface. The excitation light beam has one or more defined wavelengths. A control sets the relative positions between the carrier and the excitation light beam.

An INDEPENDENT CLAIM is included for a fluorescence scanner (10) to detect immobilized substances, on a carrier, with a light source to deliver a series of pulses of an excitation light at a defined measurement field on the **bio-chip** (15) carrier, where a system (25) detects fluorescent light from the illuminated substances between the pulses, a system gives a timed correlation between the light and detection units, and a control (30) determines the relative positions between the carrier and the light.

USE - The method and system is used for the evaluation of **bio-chips**, where immobilized substances are held on a flat carrier as fixed biological probes and/or samples bonded in the probes. The probes are nucleic acids and especially oligonucleotides e.g. single- and/or twin-strand DNA, RNA, PNA, LNA in pure or combination forms, antibodies, enzymes, haptenes, pesticides, hormones, **antibiotics**

DOC. NO. NON-CPI: N2002-374307  
DOC. NO. CPI: C2002-134986  
TITLE: Hybridization reaction result display method involves displaying A graph showing the result of hybridization of two species comprising different fluorescent pigments, for each partition on the **bio-chip**.  
DERWENT CLASS: B04 D16 S03  
INVENTOR(S): NOZAKI, Y; WATANABE, T; NAKASHIGE, R; TAMURA, T  
PATENT ASSIGNEE(S): (HISF) HITACHI SOFTWARE ENG CO LTD; (NAKA-I) NAKASHIGE R; (NOZA-I) NOZAKI Y; (TAMU-I) TAMURA T; (WATA-I) WATANABE T  
COUNTRY COUNT: 28  
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
JP 2002071688	A	20020312	(200251)*		12
EP 1190762	A2	20020327	(200251)	EN	
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI TR					
US 2002045181	A1	20020418	(200251)		
US 6453243	B1	20020917	(200264)		

## APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
JP 2002071688	A	JP 2000-265933	20000901
EP 1190762	A2	EP 2001-115172	20010622
US 2002045181	A1	US 2001-884833	20010618
US 6453243	B1	US 2001-884833	20010618

PRIORITY APPLN. INFO: JP 2000-265933 20000901

AB JP2002071688 A UPAB: 20021031

NOVELTY - Displaying results of a hybridization reaction using a control spot region on a **bio-chip** which is divided into several partitions, performing hybridization reaction of species comprising different fluorescent pigments on the **bio-chip**, and displaying graphs showing the hybridization reaction result for corresponding partitions on a screen, is new.

DETAILED DESCRIPTION - Displaying results of a hybridization reaction uses a control spot region on a **bio-chip** which is divided into several partitions, and performing hybridization reaction of species comprising different fluorescent pigments on the **bio-chip**, and displaying graphs (where the fluorescent intensity of the respective fluorescent pigments of the species are taken along vertical and horizontal **axes** of each graph, and a co-efficient of linearity is calculated for the hybridization result data from the displayed graphs) showing the hybridization reaction result for corresponding partitions on a screen.

An INDEPENDENT CLAIM is included for an experimental error evaluation method which involves using maximum, minimum and mean values of an elevation angle between the horizontal axis and a line of linearity of the hybridization result data, to evaluate a linearity error in the hybridization result.

USE - For displaying the hybridization result of two species comprising different fluorescent pigments.

ADVANTAGE - An effective visual display of the hybridization result, is achieved.

DESCRIPTION OF DRAWING(S) - The figure shows a display of control data in the **bio-chip**.

Dwg.8/17



an agent, and determining if the agent has modulated the expression of (I); (14) an isolated human protease peptide (IX) having an amino acid sequence that shares at least 70% homology with S1; and (15) an isolated nucleic acid molecule (X) encoding (IX), where (X) shares at least 80% homology with S2. WIDER DISCLOSURE - Also disclosed are the following: (a) a method for identifying orthologs and paralogs of (I); (b) a novel agent identified by screening assays using (I); (c) a protein comprising (I), and its fragments and variants; (d) non-coding fragments of (II); and (e) a kit for detecting the presence of (II) in a biological sample. BIOTECHNOLOGY - Preparation: (I) is prepared by introducing a nucleic acid sequence encoding (I) into (VII), and culturing (VII) under conditions in which (I) is expressed from the nucleotide sequence (claimed). Preferred Method: In M3, the agent is administered to (VII). Preferred Peptide: (IX) shares at least 90% homology with S1. Preferred Polynucleotide: (X) shares at least 90% homology with S2 (transcript) or 3 (genomic). ACTIVITY - None given. MECHANISM OF ACTION - Gene therapy. USE - (VIII) is useful for treating a disease or condition mediated by a human protease (claimed). (I) or (III) is useful as models for the development of human therapeutics, for identifying therapeutic proteins, as targets for development of human therapeutic agents, and as query sequence to perform a search against sequence data bases to, for e.g., identify other family members of related sequences. (I) is useful to raise antibodies or to elicit another immune response, as a reagent in assays designed to quantitatively determine levels of the protein in biological fluids, as markers for tissues in which the corresponding protein is preferentially expressed, in biological assays related to GPCRs, in drug screening assays, in cell-based or cell-free systems, to identify compounds that modulate receptor activity of the protein in its natural state, or an altered form that causes the specific disease or pathology associated with the receptor, to screen a compound for the ability to stimulate or inhibit interaction between the receptor protein and a molecule that normally interacts to the receptor protein, as bait proteins in a two-hybrid or three-hybrid assay, to provide a target for diagnosing a disease or predisposition to disease mediated by the peptide, in pharmacogenomic analysis, and for treating a disorder characterized by an absence of, in appropriate or unwanted expression of the GPCR protein. (II) is useful for isolating and purifying (I), to detect the presence of (I) in cells or tissues, to detect protein in situ, in vitro or in a cell lysate or supernatant, to assess abnormal tissue distribution or abnormal expression during development or progression of a biological condition, to assess normal and aberrant subcellular localization of cells in the various tissues in an organisms, in pharmacogenomic analysis, for tissue typing, as diagnostic tools, and for inhibiting a protein function. (III) is useful as probes, primers, and chemical intermediates, in biological assays, for constructing recombinant vectors, host cells and transgenic animals, for expressing antigenic portions of the GPCR proteins, for designing ribozymes, for monitoring the effectiveness of modulating compounds on the expression or activity of the GPCR gene in clinical trials or in a treatment regimen, in diagnostic assays for qualitative changes in GPCR nucleic acid that lead to pathology, for testing an individual for a genotype that while not necessarily causing a disease, nevertheless affects the treatment modality, as antisense constructs to control GPCR gene expression in cells, tissues and organisms, and for gene therapy in patients containing cells that are aberrant in GPCR gene expression. (VI) is useful for producing a GPCR protein or peptide, for conducting cell-based assays involving the GPCR protein or its fragment, for identifying GPCR protein mutants whose functions are affected, and to produce non-human transgenic animals. ADMINISTRATION - No administration details are given. EXAMPLE - None given. (64 pages)

**databases** BLOCKS, DOMO, PRODOM and hidden Markov model (HMM)-based protein family **databases** such as PFAM. The queries were performed using programs based on BLAST, FASTA, BLIMPS and HMMER (undefined). The Incyte cDNA sequences were assembled to produce full-length polynucleotide sequences. The full-length polynucleotide sequences were translated to derive the corresponding polypeptide sequences. Full-length polypeptide sequences were subsequently analyzed by querying against **databases**. Neurotransmitter transporter polypeptides, NTT 1-6 comprising 602, 730, 523, 649, 625 or 592 amino acids, respectively encoded by a nucleotide sequence of 2168, 2709, 2958, 2135, 1997 or 2774 base pairs defined in the specification were isolated. (123 pages)

L99 ANSWER 33 OF 42 BIOTECHDS COPYRIGHT 2002 THOMSON DERWENT AND ISI

ACCESSION NUMBER: 2002-06114 BIOTECHDS

TITLE: Novel isolated G-protein coupled receptor peptide useful for treating disorder characterized by absence of, in appropriate or unwanted expression of the receptor protein, and as immunogens to raise antibodies;  
vector-mediated gene transfer, expression in host cell, DNA chip, database, ribozyme, antibody and transgenic animal for recombinant protein production, drug screening and disease diagnosis, therapy or genetherapy

AUTHOR: WEI M; ZHAO Q; CRAVCHIK A; DI FRANCESCO V; BEASLEY E M

PATENT ASSIGNEE: APPLERA CORP

PATENT INFO: WO 2001087980 22 Nov 2001

APPLICATION INFO: WO 2000-US15957 18 May 2000

PRIORITY INFO: US 2000-634656 8 Aug 2000

DOCUMENT TYPE: Patent

LANGUAGE: English

OTHER SOURCE: WPI: 2002-075312 [10]

AB DERWENT ABSTRACT: NOVELTY - A G-protein coupled receptor (GPCR) peptide (I) comprising a 337 amino acid sequence (S1), an allelic variant or ortholog of S1 encoded by a polynucleotide hybridizing under stringent conditions to opposite **strand** of a 1014 base pair sequence (transcript) or 3 (genomic), or a fragment of S1 having at least 10 contiguous amino acids, where the sequences are fully defined in specification, is new. DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following: (1) an isolated antibody (II) that selectively binds to (I); (2) an isolated nucleic acid molecule (III) comprising a sequence that encodes S1, a sequence that encodes an allelic variant or ortholog of S1, where the sequence hybridizes under stringent conditions to the opposite **strand** of a sequence (S2) comprising 1014 base pairs fully defined in the specification (transcript) or 3 (genomic), a sequence that encodes a fragment of S1, where the fragment comprises at least 10 contiguous amino acids, or a complement of the above mentioned sequences; (3) a gene chip (IV) comprising (III); (4) a transgenic non-human animal (V) comprising (III); (5) a nucleic acid vector (VI) comprising (III); (6) a host cell (VII) containing (VI); (7) production of (I); (8) detecting (M1) the presence of (I) in a sample involves contacting the sample with a detection agent that specifically allows detection of the presence of (I) in the sample, and then detecting the presence of (I); (9) detecting (M2) the presence of (III) in a sample involves contacting the sample with an oligonucleotide that hybridizes to (III) under stringent conditions and determining whether the oligonucleotide binds to (III) in the sample; (10) identifying (M3) a modulator of (I) involves contacting (I) with an agent and determining if the agent has modulated the function or activity of (I); (11) identifying (M4) an agent that binds to (I), involves contacting (I) with an agent and assaying the contacted mixture to determine whether a complex is formed with the agent bound (I); (12) a pharmaceutical composition (VIII) comprising an agent identified by M4; (13) identifying (M5) a modulator of the expression of (I) involves contacting a cell expressing (I) with

NTT in a patient. (I) is useful for screening for a compound that modulates the activity of the polypeptide or that binds to the polypeptide. (I) is further useful as an immunogen for preparing polyclonal or monoclonal antibody by hybridoma technology. (II) is useful for screening a compound for effectiveness in altering expression of a target polynucleotide comprising the sequence of (II). A probe comprising at least 20 contiguous nucleotides of (II) is useful for assessing toxicity of a test compound, by treating a biological sample containing nucleic acids with the test compound, hybridizing the probe with nucleic acids of the treated biological sample to form a complex, quantifying the amount of hybridization complex and comparing the complex in the treated biological sample with the amount of complex in an untreated biological sample, where a difference in the amount of complex in the treated biological sample is indicative of toxicity of the test compound. (IV) is useful for detecting the presence of (I) and purifying (I) from a sample. (IV), optionally labeled is useful for diagnosing a condition or disease associated with expression of NTT in a subject or in a biological sample (all claimed). (I) and (II) and modulators of (I) are useful for diagnosis, treatment and prevention of transport, neurological and psychiatric disorders. Transport disorders include akinesia, amyotrophic lateral sclerosis, ataxia telangiectasia, cystic fibrosis, Becker's muscular dystrophy, diabetes mellitus, diabetes insipidus, myasthenia gravis, myocarditis, Parkinson's disease, prostate cancer; cardiac disorders associated with transport include angina, bradyarrhythmia, dermatomyositis, polymyositis, neurological disorders associated with transport include Alzheimer's disease, amnesia, bipolar disorder, dementia, depression, epilepsy, Tourette's disorder, schizophrenia, and other disorders associated with transport include neurofibromatosis, sickle cell anemia, Wilson's disease, cataracts, infertility, hyperglycemia, hypoglycemia, Graves' disease, goiter, Cushing's disease, hypercholesterolemia and cystinuria. Neurological disorders treatable include epilepsy, stroke, Huntington's disease, dementia, and other extrapyramidal disorder, motor neuron disorders, prion disease including kuru, metabolic disease of the nervous system, and other developmental disorders of the central nervous system, neuromuscular disorders, metabolic, endocrine and toxic myopathies, periodic paralysis, mental disorders including mood and anxiety. Psychiatric disorders include acute stress disorder, alcohol dependence, anorexia nervosa, anxiety, obsessive-compulsive disorder, panic disorder and sleep disorder. (II) is useful for creating knock in humanized animals or transgenic animals to model human disease and to detect and quantify gene expression in biopsied tissues in which expression of NTT is correlated with disease. (II) is also useful for generating hybridization probes useful in mapping the naturally occurring genomic sequence and oligonucleotide primers derived from (II) are useful to detect single nucleotide polymorphisms. NTT, fragments of it and antibodies specific for NTT are useful as elements on a **microarray** which is useful to monitor or measure protein-protein interactions, drug-target interactions and gene expression profiles. Sequences of (I) are used to analyze the proteome of a tissue or cell type. ADMINISTRATION - Administered by oral, intravenous, intramuscular, intraarterial, intramedullary, intrathecal, intraventricular, pulmonary, transdermal, subcutaneous, topical, intranasal, sublingual or rectal route at a dose of 0.1 microg-1 g. EXAMPLE - Incyte cDNAs were derived from cDNA libraries constructed using RNA isolated from brain tissue (BRAITUT02 and BRAINOT09), diseased cerebellum tissue (BRABDIR02), breast tumor tissue (BRSTTUT14), dorsal root ganglion tissue (DRGTNOT01) and normalized substantia nigra tissue (BRAGNON02). cDNA were ligated into compatible restriction enzyme sites of the polylinker of a suitable plasmid and transformed into competent Escherichia coli cells. Incyte cDNA was recovered from the plasmids and sequenced. Incyte clones 7617689CB1, 6881669CB1, 2742486CB1, 71556695CB1, 7472800CB1 and 7475553CB1 were then used to search publicly available **databases** such as GenBank primate, mammalian, and eukaryotic

single chain antibody, humanized antibody, Fab, DNA probe, DNA primer, agonist, antagonist and database for use in disease diagnosis, prevention and gene therapy, mapping, SNP, microarray, drug target and expression profiling

AUTHOR: SANJANWALA M S; WALIA N K; TRIBOULEY C M; YUE H; GANDHI A R; DING L; YAO M G; LAL P; BAUGHN M R; HAFALIA A; ELLIOTT V S; PATTERSON C; RANKUMAR J

PATENT ASSIGNEE: INCYTE GENOMICS INC

PATENT INFO: WO 2001090148 29 Nov 2001

APPLICATION INFO: WO 2000-US16283 19 May 2000

PRIORITY INFO: US 2000-228448 27 Jul 2000

DOCUMENT TYPE: Patent

LANGUAGE: English

OTHER SOURCE: WPI: 2002-097640 [13]

AB DERWENT ABSTRACT: NOVELTY - An isolated human neurotransmitter transporter polypeptide (I), (NTT) 1-6, comprising a sequence (S1) of 602, 730, 523, 649, 625 or 592 amino acids defined in the specification, a naturally occurring polypeptide comprising an amino acid sequence 90% identical to (S1), a biologically active or immunogenic fragment of (S1), is new. DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following: (1) an isolated polynucleotide (II) encoding (I) and comprising a sequence (S2) of 2168, 2709, 2958, 2135, 1997 or 2774 base pairs (bp) defined in the specification, a naturally occurring polynucleotide comprising a polynucleotide sequence 90% identical to (S2), a polynucleotide complementary to (II) or an RNA equivalent of (II); (2) a recombinant polynucleotide (III) comprising a promoter sequence operably linked to (II); (3) a cell transformed with (III); (4) a transgenic organism comprising (III); (5) method of producing (I); (6) an isolated antibody (IV) which specifically binds to (I); (7) an isolated polynucleotide comprising at least 60 contiguous nucleotides of (II); (8) detecting (M1) a target polynucleotide having the sequence of (II) in a sample, by: (a) hybridizing the sample with a probe comprising 20 contiguous nucleotides comprising a sequence complementary to the target polynucleotide in the sample, where the probe specifically hybridizes to the target polynucleotide under conditions where a hybridization complex is formed between the probe and the target polynucleotide or its fragments, or by amplifying the target polynucleotide or its fragment by PCR; and (b) detecting the presence or absence of the hybridization complex or the amplified product, and, optionally, if present the amount of the complex or the amplified product; (9) an antibody (monoclonal) produced by using (I); and (10) a composition comprising (I), an agonist or antagonist compound identified using (I), (IV) or the above antibody. WIDER DISCLOSURE - Variants of (I) and (II) are also disclosed. BIOTECHNOLOGY - Preparation: (I) is produced by culturing a cell transformed with (III), under conditions suitable for expression of the polypeptide and recovering the expressed polypeptide. (IV) is produced by screening Fab expression library or a recombinant immunoglobulin library (claimed). Preferred Antibody: (IV) is a chimeric, single chain, Fab, F(ab')<sub>2</sub> fragment or a humanized antibody. Preferred Method: In (M1), the probe comprises at least 60 contiguous nucleotides. ACTIVITY - Antidiabetic; Antiparkinsonian; Antianginal; Neuroprotective; Nootropic; Antidepressant; Anticonvulsant; Neuroleptic; Antianemic; Ophthalmological; Antithyroid; Cerebroprotective; Tranquilizer; Vasotropic; Cytostatic; Antiarrhythmic; Dermatological; Antilipemic; Muscular-Gen; Antimicrobial; Cardiant; Antisickling; Antiinfertility; Endocrine-Gen. MECHANISM OF ACTION - Gene therapy; neurotransmitter transporter polypeptide modulator. No supporting data is given. USE - (I) is useful for screening a compound for effectiveness as an agonist or antagonist of (I), by exposing a sample comprising (I) to a compound and detecting agonist or antagonist activity in the sample. (I), the identified agonist and antagonist are useful for treating a disease or condition associated with decreased or overexpression of functional

a nucleotide sequence that encodes AA1, an allelic variant or ortholog of AA1, a fragment of AA1 comprising at least 10 contiguous amino acids, or a their complements; (3) a gene chip, a transgenic non-human animal, and a nucleic acid vector comprising (II); (4) a host cell containing the vector; (5) a method of producing the peptide by introducing a nucleotide sequence encoding any of the amino acid sequences defined above into a host cell, and culturing the host cell under conditions in which the peptides are expressed; (6) method of detecting the presence the peptide in a sample by contacting the sample with a detection agent that specifically allows detection of the presence of the peptide in the sample; (7) a method of detecting the presence of (II) in a sample by contacting the sample with an oligonucleotide that hybridizes to (II) under stringent conditions and determining whether the oligonucleotide binds to the nucleic acid in the sample; (8) a method of identifying a modulator of (I) by contacting the peptide with an agent and determining if the agent has modulated the function or activity of the peptide; (9) a method of identifying an agent that binds to (I), by contacting the peptide with an agent and assaying the contacted mixture to determine whether a complex is formed with the agent bound to the peptide; (10) a pharmaceutical composition comprising an agent identified by the method of (9) and a carrier; (11) a method of treating a disease or condition mediated by a human kinase protein, by administering to a patient an agent identified from (9); (12) a method for identifying a modulator of the expression of (I) by contacting a cell expressing (I), with an agent, and determining if the agent has modulated the expression of (I); (13) an isolated human kinase peptide having an amino acid sequence that shares at least 70% homology with AA1; and (14) an isolated nucleic acid molecule encoding a human kinase peptide having at least 80% homology with S1 or S2. BIOTECHNOLOGY - Preferred Sequences: The peptide preferably shares at least 90% homology to AA1. The nucleic acid preferably shares at least 90% homology to S1 or S2. Preferred Method: The agent is administered to a host cell comprising an expression vector that expresses the peptide. ACTIVITY - None given. MECHANISM OF ACTION - Peptide therapy; gene therapy. USE - The peptide and nucleic acid sequences can be used as models for the development of human therapeutic targets, aid in the identification of therapeutic proteins, and serve as targets for the development of human therapeutic agents that modulate kinase activity in cells and tissues that express the kinase. The nucleic acid and protein sequences may be further used as query sequence in performing a search against sequence databases to identify other family members or related sequences, as probes or primers, for constructing recombinant vectors, host cells and transgenic animals expressing the nucleic acids, as antisense construct to control kinase gene expression in cells, tissues and organisms, The proteins are useful for raising antibodies or to elicit another immune response, as a reagent in assays designed to quantitatively determine levels of the protein in biological fluids, as markers for tissues in which the corresponding protein is preferentially expressed, in drug screening assays, in screening for compounds for the ability to stimulate or inhibit interaction between the kinase protein and a molecule that normally interacts with the kinase protein, and for treating a disorder characterized by an absence of, inappropriate, or unwanted expression of the protein. EXAMPLE - No examples given. (66 pages)

L99 ANSWER 32 OF 42 BIOTECHDS COPYRIGHT 2002 THOMSON DERWENT AND ISI  
ACCESSION NUMBER: 2002-07486 BIOTECHDS

TITLE: Novel human neurotransmitter transporter polypeptides and polynucleotides for diagnosing, preventing or treating transport, neurological and psychiatric disorders and for identifying modulators of therapeutic use;  
vector-mediated recombinant protein gene transfer and expression in Escherichia coli, transgenic animal model construction, monoclonal antibody, chimeric antibody,

transferase. (I) is also useful as bait proteins in a two-hybrid assay or a three-hybrid assay to identify other proteins that bind, interact with amino transferase. (I) is also useful for providing a target for diagnosing a disease or predisposition to disease mediated by the peptide, and targets for diagnosing active protein activity, diseases and predisposition to a disease, in pharmacogenomic analysis, and for treating a disorder characterized by absence of, inappropriate or unwanted expression of (I). Ab is useful for isolating proteins by standard technique, to assess expression of proteins in disease states, assessing normal and aberrant subcellular localization of cells in various tissues of an organism, in pharmacogenomic analysis, in tissue typing and for protein inhibition. (II) is useful as probes to isolate full length cDNA and genomic clones encoding (I), as primers for PCR amplification of any given region of nucleic acid molecule and for synthesizing antisense molecules of desired length and sequence for constructing recombinant vectors, for expressing antigenic portions of the proteins, as probes for determining chromosomal localization of the nucleic acid molecules by means of in situ hybridization methods, for making vectors containing the gene regulatory regions of (II), for designing ribozymes corresponding to all or a part of the mRNA produced from (II), for constructing host cells and transgenic animals, and as hybridization probes for determining the presence, level, form and distribution of nucleic acid expression. (II) is also useful for monitoring the effectiveness of modulating compounds on the expression or activity of aminotransferase gene in clinical trials or treatment regimen, and for qualitative changes in aminotransferase nucleic acid expression. (II) is also useful for testing individual for a genotype, for displaying genetic variation that affect treatment and as antisense constructs. (VI) is useful for conducting cell-based assays, for identifying aminotransferase protein mutants, and for producing non-human transgenic cells. ADMINISTRATION - No administration details given. EXAMPLE - No data provided. (62 pages)

L99 ANSWER 31 OF 42 BIOTECHDS COPYRIGHT 2002 THOMSON DERWENT AND ISI

ACCESSION NUMBER: 2002-06121 BIOTECHDS

TITLE: Human kinase proteins and nucleic acids encoding the proteins, useful for developing human therapeutic targets, or for treating a disorder characterized by an absence, inappropriate, or unwanted expression of the protein; vector-mediated gene transfer, expression in host cell, antisense oligonucleotide, antibody and transgenic animal for recombinant protein production, drug screening and disease therapy or genetherapy

AUTHOR: WEI M; ZHU S; WOODAGE T; DI FRANCESCO V; BEASLEY E M

PATENT ASSIGNEE: APPLERA CORP

PATENT INFO: WO 2001090328 29 Nov 2001

APPLICATION INFO: WO 2000-US16760 24 May 2000

PRIORITY INFO: US 2000-691861 18 Oct 2000

DOCUMENT TYPE: Patent

LANGUAGE: English

OTHER SOURCE: WPI: 2002-075372 [10]

AB DERWENT ABSTRACT: NOVELTY - Isolated human kinase proteins (comprising a fully defined 367 amino acid sequence (AA1) given in the specification) and encoding nucleic acids, are new. DETAILED DESCRIPTION - An isolated peptide (I) consisting of sequence selected from: (a) a fully defined 367 amino acid sequence (AA1) given in the specification; (b) an allelic variant or ortholog of (AA1) encoded by a nucleic acid molecule that hybridizes under stringent conditions to the opposite strand of a nucleic acid having a defined 1104 (S1) or 9862 (S2) bp sequence given in the specification; and (c) a fragment of (AA1) comprising at least 10 contiguous amino acids. INDEPENDENT CLAIMS are also included for the following: (1) an isolated antibody that selectively binds to the peptide defined above; (2) an isolated nucleic acid (II) consisting or comprising

defined in the specification), or a fragment of at least 10 contiguous amino acids of (S1), is new. DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following: (1) an isolated antibody (Ab) that selectively binds to (I); (2) an isolated nucleic acid molecule (II) consisting of a nucleotide sequence that encodes (I), or its complement; (3) a gene chip (III) comprising (II); (4) a transgenic non-human animal (IV) comprising (II); (5) a nucleic acid vector (V) comprising (II); (6) a host cell (VI) containing (V); (7) production of (I); (8) determining the presence of (I) in a sample, by contacting the sample with a detection agent that specifically allows detection of the presence of (I) in the sample and then detecting the presence of (I); (9) detecting the presence of (II) in a sample, by contacting the sample with an oligonucleotide that hybridizes to (II) under stringent conditions and determining whether the oligonucleotide binds to (II) in the sample; (10) a pharmaceutical composition (PC) comprising an agent that binds (I) and identified using (I); (11) identifying a modulator of the expression of (I), by contacting a cell expressing (I) with an agent, and determining if the agent has modulated the expression of (I); (12) an isolated human aminotransferase peptide having an amino acid sequence that shares at least 70% homology with S1; and (13) an isolated nucleic acid molecule encoding a human aminotransferase peptide sharing at least 80% homology with S2. WIDER DISCLOSURE - The following are also disclosed: (1) other end point assays to identify compounds that modulate aminotransferase activity; (2) novel agents identified by the above said method; (3) kits using antibodies to detect the presence of a protein in a biological sample; (4) kits for detecting the presence of aminotransferase nucleic acid in a biological sample; and (5) compartmentalized kits to receive one or more containers, comprising (II), wash reagents and reagents capable of detecting the presence of bound (II). BIOTECHNOLOGY - Preparation: (I) is prepared by introducing a nucleotide sequence encoding S1 into (VI), and culturing (VI) under conditions in which (I) is expressed from the nucleotide sequence (claimed). Preferred Sequence: (I) shares at least 90% homology with S1. (II) shares at least 90% homology with S2. ACTIVITY - None given. MECHANISM OF ACTION - Gene therapy; vaccine. No supporting data given. USE - (I) is useful for identifying a modulator of (I), by contacting (I) with an agent, preferably the agent is administered to a host cell comprising an expression vector that expresses (I), and determining if the agent has modulated the function or activity of (I). (I) is also useful for (11) identifying an agent that binds to (I), by contacting (I) with an agent and assaying the contacted mixture to determine whether a complex is formed with the agent bound to (I). A pharmaceutical composition (PC), is useful for treating a disease or condition mediated by a human aminotransferase protein (all claimed). (I) and (II) are useful as models for the development of human therapeutic targets, aid in the identification of therapeutic proteins and serve as targets for the development of human therapeutic agents that modulate amino transferase activity in cells and tissues that express the amino transferase. (I) and (II) are also useful as query sequences to perform a search against sequence databases to identify other family members or related sequences. (I) is also useful to raise antibodies to elicit another immune response, as a reagent in assays designed to quantitatively determine levels of the protein in biological fluids and as tissue markers. (I) is also useful for biological assays, drug screening assays, to identify compounds that modulate aminotransferase activity of the protein in its natural state or altered form that causes a specific disease or pathology associated with the amino transferase, to screen compound for the ability to stimulate or inhibit interaction between amino transferase protein that normally interacts with the aminotransferase, and in competition binding assays in methods designed to discover compounds that interact with aminotransferase. The modulators of aminotransferase thus identified are useful for treating a subject with a disorder mediated by the amino transferase pathway for treating cells or tissues that express the amino

development of human therapeutics and diagnostic compositions, and as models for the development of human therapeutic targets. (I) serves as targets for identifying agents for use in mammalian therapeutic applications, e.g. a human drug, particularly in modulating a biological or pathological response in a cell or tissue that expresses the transporter. (I) and (II) are useful for treating, preventing and/or diagnosing dicarboxylate transporter related diseases such as kidney disorder, in drug screening assays, and as query sequence to perform a search against sequence databases. (I) is also useful to raise antibodies, as a reagent in assays designed to quantitatively determine levels of the protein in biological fluids, as markers for tissues in which the corresponding protein is expressed, and to identify the binding partner/ligand to develop a system to identify inhibitors of the binding interaction. (II) is useful for identifying other family members or related sequences and in pharmacogenomics. (II) is also useful as primer intermediate and as hybridization probe for mRNA and genomic DNA to isolate full-length cDNA, to synthesize antisense molecules of desired length and sequences, for constructing recombinant vectors, for expressing antigenic portions of the proteins, as probes for determining the chromosomal positions of the nucleic acid molecule, for constructing transgenic animals, for designing ribozymes, and as hybridization probes for determining the presence, level, form and distribution of nucleic acid expression. (II) is also useful for monitoring the effectiveness of modulating compounds on the expression or activity of the transporter gene in clinical trials or in a treatment regimen, and in diagnostic assays, and as antisense constructs to control transporter gene expression in cells, tissues and organisms. (IV) is useful for conducting cell-based assays, for identifying transporter protein mutants and to produce non-human transgenic animals useful for studying the function of a transporter protein and identifying and evaluating modulators of the protein activity. (V) is useful as immunogen, to isolate and purify the proteins and to detect the presence of the proteins in cells or tissues to determine the pattern of the expression of the protein in situ, in vitro, or in a cell lysate or supernatant, and to assess abnormal tissue distribution or expression during development or progression of a biological condition. (V) is also useful to assess normal and aberrant subcellular localization of cells in various tissues in an organism, in pharmacogenomic analysis, tissue typing, and as an immunological marker for aberrant protein expression. (49 pages)

L99 ANSWER 30 OF 42 BIOTECHDS COPYRIGHT 2002 THOMSON DERWENT AND ISI

ACCESSION NUMBER: 2002-06171 BIOTECHDS

TITLE: Novel human amino transferase polypeptide useful for identifying agents that modulate amino transferase activity, for treating a subject with a disorder mediated by the amino transferase pathway;  
recombinant protein gene production, non-human transgenic animal, and vector expression in host cell useful in gene therapy

AUTHOR: YAN C; GAN W; WOODAGE T; KETCHUM K; DI FRANCESCO V; BEASLEY E M

PATENT ASSIGNEE: APPLERA CORP

PATENT INFO: WO 2001092490 6 Dec 2001

APPLICATION INFO: WO 2000-US17292 30 May 2000

PRIORITY INFO: US 2001-801874 9 Mar 2001

DOCUMENT TYPE: Patent

LANGUAGE: English

OTHER SOURCE: WPI: 2002-130532 [17]

AB DERWENT ABSTRACT: NOVELTY - An isolated human amino transferase polypeptides (I) comprising a sequence of (S1) of 380 amino acids, an allelic variant or ortholog of (SI) encoded by a nucleotide molecule that hybridizes under stringent conditions to the opposite strand of a sequence (S2) comprising 1517 or 9377 nucleotides (S1 and S2 are fully



host cells and transgenic animals, and for designing ribozymes. The nucleic acid molecules are also useful for monitoring effectiveness of modulating compounds on the expression or activity of drug metabolizing enzyme gene in clinical trials or in treatment regimen, and for testing an individual for a genotype that while not necessarily causing the disease nevertheless affects the treatment modality. (III) also provides vectors for gene therapy in patients containing cells that are aberrant in drug metabolizing enzyme gene expression. EXAMPLE - None given. (65 pages)

L99 ANSWER 29 OF 42 BIOTECHDS COPYRIGHT 2002 THOMSON DERWENT AND ISI

ACCESSION NUMBER: 2002-15954 BIOTECHDS

TITLE: New human transporter peptide related to sodium-dependent dicarboxylate transporter subfamily, useful for identifying modulators of the transporter peptide and developing human therapeutic and diagnostic compositions;  
vector-mediated recombinant protein gene transfer and expression in host cell for kidney disorder diagnosis, prevention and gene therapy

AUTHOR: CHATURVEDI K; WEI M; KETCHUM K A; DI FRANCESCO V; BEASLEY E M

PATENT ASSIGNEE: CHATURVEDI K; WEI M; KETCHUM K A; DI FRANCESCO V; BEASLEY E M

PATENT INFO: US 2002019028 14 Feb 2002

APPLICATION INFO: US 2000-729094 13 Jun 2000

PRIORITY INFO: US 2000-729094 5 Dec 2000

DOCUMENT TYPE: Patent

LANGUAGE: English

OTHER SOURCE: WPI: 2002-328584 [36]

AB DERWENT ABSTRACT: NOVELTY - An isolated human transporter peptide (I) related to sodium-dependent dicarboxylate transporter subfamily, comprising a sequence (S1) of 568 amino acids, its allelic variant or ortholog encoded by a nucleic acid molecule that hybridizes to opposite **strand** of a nucleic acid molecule having a sequence (S2) of 2223 or 32816 base pairs fully defined in specification, or a fragment of (S1) having 10 contiguous amino acids, is new. DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following: (1) an isolated nucleic acid molecule encoding human transporter peptide, sharing at least 80% homology with (S2); (2) an isolated nucleic acid molecule (II) comprising a nucleotide sequence encoding (I), or its complement; (3) a gene chip comprising (II); (4) a transgenic non-human animal comprising (II); (5) a nucleic acid vector (III) comprising (II); (6) a host cell (IV) containing (III); (7) producing (I); (8) an isolated antibody (V) that selectively binds to (I); (9) detecting the presence of (I) in a sample, by contacting the sample with a detection agent that specifically allows detection of the presence of the peptide in the sample, and then detecting the presence of the peptide; (10) detecting the presence of (II) in a sample, by contacting the sample with an oligonucleotide that hybridizes to the nucleic acid molecule under stringent conditions, and determining whether the oligonucleotide binds to the nucleic acid molecule in the sample; (11) a pharmaceutical composition comprising an agent identified by using (I); and (12) an isolated human transporter peptide (VI) having an amino acid sequence that shares 70% homology with (S1). WIDER DISCLOSURE - Also disclosed are: (1) kit comprising (V), useful for detecting the presence of (I) in a biological sample; and (2) non-coding fragments of (II). BIOTECHNOLOGY - Preparation: (I) is produced by culturing (IV) under conditions in which the peptides are expressed from the nucleotide sequence. Preferred Peptide: (VI) shares at least 90% homology with (S1). Preferred Nucleic Acid: The nucleic acid shares at least 90% homology with S2. ACTIVITY - Nephrotropic. MECHANISM OF ACTION - Modulator of (I); Gene therapy. No supporting data is given. USE - (I) is useful for identifying a modulator of the function, activity or expression of the peptide or an agent that binds to the peptide. The agent identified is useful for treating a disease or condition mediated by a human transporter protein (claimed). (I) and (II) are useful for the

and determining if the agent has modulated the function or activity of the peptide; (11) identifying an agent that binds to (I) comprising contacting (I) with an agent and assaying the contacted mixture to determine whether a complex is formed with the agent bound to (I); (12) a pharmaceutical composition (V) comprising an agent that binds to (I), and identified using (I) (comprising a sequence of (S2), its allelic variant or ortholog or fragment), and a carrier; (13) treating a disease or condition mediated by (I) comprising administering (V); (14) an isolated human drug metabolizing enzyme (VI) having an amino acid sequence that shares at least 70 % homology with (S2); and (15) an isolated nucleic acid molecule (VII) encoding a human drug metabolizing enzyme peptide, which shares at least 80 % homology with (S1) or (S3). WIDER DISCLOSURE - The following are disclosed: (1) chimeric or fusion proteins comprising (I); (2) agents identified using screening methods involving (I); (3) non-coding fragments of a nucleic acid molecule having a sequence of (S1) or (S3); (4) a kit comprising (II) for detecting (I) comprising an amino acid sequence of (S2), its allelic variant or ortholog or fragment; and (5) kits for detecting the presence of drug metabolizing enzyme nucleic acid in a biological sample. BIOTECHNOLOGY - Preparation: (I) is prepared by standard recombinant techniques (claimed). Preferred Molecules: (VI) shares 90 % homology with (S2), and (VII) shares at least 90 % homology with (S1) or (S3). Preferred Method: In (10), the agent is administered to a host cell comprising an expression vector that expresses (I). ACTIVITY - None given. MECHANISM OF ACTION - Gene therapy; (I) expression or activity modulator. No biological data is given. USE - (I) comprising an amino acid sequence of (S2), its allelic variant or ortholog or fragment, is useful for identifying a modulator of a human drug metabolizing enzyme. (I) comprising an amino acid sequence of (S2), its allelic variant or ortholog or fragment is also useful for identifying an agent that binds to it. A pharmaceutical composition (V) comprising an agent that binds to (I) is useful for treating a disease or condition mediated by human drug metabolizing enzyme (all claimed). (I) and a nucleic acid (III) that encodes (I) can be used as models for the development of human therapeutic targets, aid in the identification of therapeutic proteins and serve as targets for the development of human therapeutic agents that modulate the drug metabolizing enzyme activity in cells and tissues expressing the enzyme. (I) and (III) can be used as a query sequence to perform a search against sequence databases to, for example, identify other family members or related sequences. (I) is used to raise antibodies or to elicit another immune response, as a reagent in assays designed to quantitatively determine levels of the protein in biological fluids, and as markers for tissues in which the corresponding protein is preferentially expressed. The drug metabolizing enzymes isolated from humans and their human/mammalian orthologs serve as targets for identifying agents for use in mammalian therapeutic applications, and biological assays related to drug metabolizing enzymes that are related to members of the cytochrome P450 IVF subfamily. (I) is also useful in drug screening assays. The proteins can also be used in screening assays to screen a compound for its ability to stimulate or inhibit interaction between drug metabolizing enzyme and a molecule that normally interacts with the drug metabolizing enzyme. The proteins also provide a target for diagnosing a disease or predisposition to disease mediated by the peptide, and in pharmacogenomic analysis. The peptides are also useful for treating a disorder characterized by absence of, inappropriate or unwanted expression of the protein. An antibody (II) against (I) is useful for isolating (I), purifying (I), and to assess expression of (I) in active stages of a disease, or in an individual with a predisposition towards disease related to the protein's function. The antibodies are also useful for assessing normal and aberrant subcellular localization of cells in various tissues in an organism, in pharmacogenomic analysis, for tissue typing and for inhibiting protein function. (III) is useful as probes, primers, chemical intermediates and in biological assays. The nucleic acid molecules are useful for constructing recombinant vectors,

transporter activity of the protein in its natural state or altered form that causes a specific disease or pathology associated with the transporter; as target for diagnosing a disease or predisposition to disease mediated by the peptide; and in pharmacogenomic analysis. The nucleic acids are useful as hybridization probes or primers; in monitoring the effectiveness of modulating compounds on the expression or activity of the transporter gene in clinical trials or treatment regimen; in diagnostic assays for qualitative changes in transporter nucleic acid expression; and as antisense constructs. (207 pages)

L99 ANSWER 28 OF 42 BIOTECHDS COPYRIGHT 2002 THOMSON DERWENT AND ISI

ACCESSION NUMBER: 2002-14105 BIOTECHDS

TITLE: New human drug metabolizing enzyme that is related to the cytochrome P450 IVF drug metabolizing enzyme subfamily useful for development of human therapeutic targets and as targets for developing therapeutics;

recombinant enzyme protein, antibody, transgenic animal, and ribozyme use in disease therapy and gene therapy

AUTHOR: GUEGLER K; BRANDON R C; KETCHUM K A; DI FRANCESCO V; BEASLEY E M

PATENT ASSIGNEE: GUEGLER K; BRANDON R C; KETCHUM K A; DI FRANCESCO V; BEASLEY E M

PATENT INFO: US 2002022254 21 Feb 2002

APPLICATION INFO: US 2000-738878 28 Jul 2000

PRIORITY INFO: US 2000-738878 18 Dec 2000

DOCUMENT TYPE: Patent

LANGUAGE: English

OTHER SOURCE: WPI: 2002-255651 [30]

AB DERWENT ABSTRACT: NOVELTY - An isolated human drug metabolizing enzyme (I) that is related to the cytochrome P450 IVF drug metabolizing enzyme subfamily, consisting or comprising a sequence of 553 amino acids (S2), given in the specification, or its fragment comprising 10 contiguous amino acids, or an amino acid sequence of an allelic variant or ortholog of the amino acid sequence of (S2), is new. DETAILED DESCRIPTION - A new isolated human drug metabolizing enzyme (I) consists or comprises of: (i) an amino acid sequence of (S2); (ii) an amino acid sequence of an allelic variant or an ortholog of (S2), where the allelic variant or ortholog is encoded by a nucleic acid molecule that hybridizes under stringent conditions to the opposite strand of a nucleic acid molecule having a sequence of 1662 nucleotides (S1) (cDNA sequence) or 30175 nucleotides (S3) (genomic sequence), given in the specification; (iii) a fragment of an amino acid sequence of (S2), comprising 10 contiguous amino acids. INDEPENDENT CLAIMS are also included for the following: (1) an isolated antibody (II) that selectively binds to (I) comprising the amino acid sequence of (S2), its allelic variant or ortholog, or fragment; (2) an isolated nucleic acid molecule (III) consisting or comprising of a nucleotide sequence that encodes (I) or a nucleotide sequence that is the complement of the nucleotide sequence encoding (I); (3) a gene chip comprising (III) that comprises a nucleotide sequence encoding (I), or its complement; (4) a transgenic non-human animal comprising (III) that comprises a nucleotide sequence encoding (I), or its complement; (5) a nucleic acid vector (IV) comprising (III) that comprises a nucleotide sequence encoding (I), or its complement; (6) a host cell comprising (IV); (7) producing (I) comprising introducing a nucleotide sequence encoding (I) into a host cell and culturing the host cell to produce (I); (8) detecting the presence of (I) in a sample comprising contacting the sample with a detection agent that specifically allows detection of the presence of the peptide in the sample; (9) detecting the presence of (III) in a sample comprising contacting the sample with an oligonucleotide that hybridizes to the nucleic acid molecule under stringent conditions and determining whether the oligonucleotide binds to the nucleic acid molecule in the sample; (10) identifying a modulator of (I) comprising contacting (I) with an agent

in the specification; (b) an allelic variant or an ortholog of P1; (c) a fragment of P1 comprising at least 10 contiguous amino acids; or (d) a sequence that is 70% homologous to P1. DETAILED DESCRIPTION - A new isolated peptide (I) comprising or consisting of: (a) a fully defined sequence of 543 amino acids (P1) given in the specification; (b) an allelic variant or an ortholog of P1 encoded by a nucleic acid molecule that hybridizes under stringent conditions to the opposite **strand** of a 2065 (S1) or 43306 (S2) base pair sequence given in the specification; (c) a fragment of P1 comprising at least 10 contiguous amino acids; or (d) a sequence that is 70% homologous to P1. INDEPENDENT CLAIMS are also included for the following: (1) an isolated antibody that selectively binds to (I); (2) an isolated nucleic acid molecule (II) comprising or consisting of: (a) a sequence encoding P1; (b) a sequence encoding an allelic variant or ortholog of P1, where the nucleotide sequence hybridizes under stringent conditions to the opposite **strand** of S1 or S2; (c) a sequence encoding a fragment of P1 consisting of at least 10 contiguous amino acids; or (d) a complement of (a)-(c); (3) a gene chip comprising (II); (4) a transgenic non-human animal comprising (II); (5) a nucleic acid vector comprising (II); (6) a host cell containing the vector; (7) producing (I); (8) detecting the presence of (I) or (II) in a sample; (9) identifying a modulator of (I) by contacting the (I) with an agent and determining if the agent has modulated the function or activity of (I); (10) identifying an agent that binds to (I) by contacting (I) with an agent and assaying the contacted mixture to determine if a complex is formed with the agent bound to the peptide; (11) a pharmaceutical composition comprising an agent identified from (10) and a pharmaceutical carrier; (12) treating a disease or condition mediated by a human transporter protein by administering to the patient an agent identified from (10); (13) identifying a modulator of the expression of (I) by contacting a cell expressing the peptide with an agent, and determining if the agent has modulated the expression of the (I); and (14) an isolated nucleic acid molecule encoding a human transporter peptide, and having at least 80% homology with S1 or S2. BIOTECHNOLOGY - Preparation: (I) is produced by introducing a nucleotide sequence encoding any of the amino acid sequences defined above into a host cell, and culturing the host cell for the expression of the peptides from the nucleotide sequence. Preferred Method: Detecting the presence of (I) in a sample comprises contacting the sample with a detection agent that specifically allows the detection of the presence of the peptide in the sample. Detecting the presence of (II) in a sample comprises contacting the sample with an oligonucleotide that hybridizes to the nucleic acid molecule under stringent conditions, and determining if the oligonucleotide binds to the nucleic acid molecule in the sample. Identifying a modulator of (I) comprises contacting the peptide with an agent and determining if the agent has modulated the function or activity of the peptide. The agent is administered to a host cell comprising an expression vector that expresses the peptide. Preferred Sequences: The isolated human transporter peptide preferably shares at least 90% homology with P1. The isolated nucleic acid molecule encoding a human transporter peptide preferably shares at least 90% homology with S1 or S2. ACTIVITY - None given in the source material. MECHANISM OF ACTION - None given in the source material. USE - The peptide sequences and the nucleic acid sequences encoding these peptides can be used as models for the development of human therapeutic targets, aid in the identification of therapeutic proteins, and serve as targets for the development of human therapeutic agents that modulate transporter activity in cells and tissues that express the transporter. These sequences may also be used as query sequence in database searches to identify other family members or related sequences. The proteins may be used to raise antibodies or to elicit immune response; as a reagent in assays designed to quantitatively determine protein levels in biological fluids; as markers for tissues in which the corresponding protein is expressed; in drug screening assays in cell-based or cell-free systems; to identify compounds that modulate

an agent identified by the method of (11) and a pharmaceutical carrier; (13) treating a disease or condition mediated by a human transporter protein by administering to an agent identified in (11); (14) identifying a modulator of the expression of (I) by contacting a cell expressing (I) with an agent, and determining if the agent has modulated peptide expression; (15) an isolated human transporter peptide having an amino acid sequence having at least 70% homology with (P1); and (16) an isolated nucleic acid molecule encoding a human transporter peptide and having at least 80% homology with S1 or S2. BIOTECHNOLOGY - Preparation: (I) is produced by introducing a nucleotide sequence encoding an amino acid sequence as defined above into a host cell, and culturing the host cell for the expression of the peptide. Preferred Method: Identifying a modulator of (I) comprises contacting (I) with an agent, and determining if peptide function or activity is modulated. The agent is administered to a host cell comprising an expression vector that expresses the peptide. Preferred Sequences: The human transporter peptide preferably shares at least 90% homology with P1. The nucleic acid encoding the human transporter peptide preferably shares at least 90% with S1 or S2. ACTIVITY - None given in the source material. MECHANISM OF ACTION - None given in the source material. USE - The peptides and nucleic acids encoding the peptides may be used as models for the development of human therapeutic targets, in identifying therapeutic proteins, as targets for the development of human therapeutic agents that modulate transporter activity in cells and tissues that express the transporter, and as query sequence in database searches to identify other family members or related sequences. The proteins may further be used to raise antibodies or to elicit immune response, as a reagent in assays designed to quantitatively determine protein levels in biological fluids, as markers for tissues in which the corresponding protein is preferentially expressed, in drug screening assays in cell-based or cell-free systems, to identify compounds that modulate transporter activity, to screen a compound for the ability to stimulate or inhibit interaction between the transporter protein and a molecule that normally interacts with the transporter protein, as target for diagnosing a disease or predisposition to disease mediated by the peptide, in pharmacogenomic analysis, and for treating a disorder characterized by the absence or unwanted expression of the protein. The nucleic acids are useful as primers and probes, for monitoring the effectiveness of modulating compounds on the expression or activity of the transporter gene in clinical trials or treatment regimen, in diagnostic assays for qualitative changes in transporter nucleic acid expression, for testing an individual for a genotype which does not necessarily cause the disease but nevertheless affects treatment modality, and as antisense constructs. (181 pages)

L99 ANSWER 27 OF 42 BIOTECHDS COPYRIGHT 2002 THOMSON DERWENT AND ISI

ACCESSION NUMBER: 2002-12895 BIOTECHDS

TITLE: New human transporter proteins and nucleic acids, useful as models in the development of human therapeutic agents, in identifying therapeutic proteins, or as query sequence in database searches to identify related sequences;  
recombinant potassium channel subfamily protein and encoding gene or antisense construct for use in prevention, diagnosis and therapy of disease

AUTHOR: GUEGLER K; KETCHUM K A; DI FRANCESCO V; BEASLEY E M

PATENT ASSIGNEE: PE CORP NY

PATENT INFO: WO 2002024748 28 Mar 2002

APPLICATION INFO: WO 2000-US29211 19 Sep 2000

PRIORITY INFO: US 2000-729920 6 Dec 2000

DOCUMENT TYPE: Patent

LANGUAGE: English

OTHER SOURCE: WPI: 2002-351999 [38]

AB DERWENT ABSTRACT: NOVELTY - A new isolated peptide (I) comprising or consisting of: (a) a fully defined sequence of 543 amino acids (P1) given

and serve as targets for the development of human therapeutic agents that modulate nuclear hormone receptor activity in cells and tissues that express the nuclear hormone receptor. The nucleic acids may be used as query sequence to perform searches against sequence databases to identify family members or related sequences, as probes or primers, to construct recombinant vectors, to identify compounds that modulate nuclear hormone receptor nucleic acid expression, in gene therapy, and as antisense constructs to control nuclear hormone receptor gene expression in cells, tissues or organisms. The polypeptides can be used to raise antibodies or to elicit an immune response, as a reagent in assays designed to determine protein levels in biological fluids, as markers for tissues in which corresponding protein is expressed, to identify binding partner/ligand to develop a system for the identification of inhibitors of the binding reaction, in drug screening assays, and to identify compounds that modulate protein activity. EXAMPLE - No relevant example given in the source material. (73 pages)

L99 ANSWER 26 OF 42 BIOTECHDS COPYRIGHT 2002 THOMSON DERWENT AND ISI

ACCESSION NUMBER: 2002-12896 BIOTECHDS

TITLE: New human transporter proteins and nucleic acid encoding the protein, useful as models in developing therapeutic targets, in identifying therapeutic proteins, or as query sequences in database searches to identify related sequences;  
recombinant protein and encoding sense or antisense gene for use in disease therapy and gene therapy, disease diagnosis, drug screening and pharmacogenomics

AUTHOR: CHANDRAMOULISWARAN I; YAN C; GUEGLER K; WEI M; DI FRANCESCO V; BEASLEY E M

PATENT ASSIGNEE: PE CORP NY

PATENT INFO: WO 2002024749 28 Mar 2002

APPLICATION INFO: WO 2000-US29217 20 Sep 2000

PRIORITY INFO: US 2000-742312 22 Dec 2000

DOCUMENT TYPE: Patent

LANGUAGE: English

OTHER SOURCE: WPI: 2002-352000 [38]

AB DERWENT ABSTRACT: NOVELTY - An isolated peptide (I) comprising or consisting of: (a) a fully defined sequence of 807 amino acids (P1) given in the specification; (b) an allelic variant or an ortholog of P1 encoded by a nucleic acid molecule that hybridizes under stringent conditions to the opposite **strand** of a defined sequence of 2424 (S1) or 147309 (S2) bp given in the specification; (c) a fragment of P1 comprising at least 10 contiguous amino acids, is new. DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following: (1) an isolated antibody that selectively binds to (I); (2) an isolated nucleic acid molecule (II) comprising or consisting of a sequence: (a) encoding P1; (b) encoding an allelic variant or an ortholog of P1, where the nucleic acid sequence hybridizes under stringent conditions to the opposite **strand** of a S1 or S2; (c) encoding a fragment of P1 which comprises at least 10 contiguous amino acids; or (d) complementary to (a)-(c); (3) a gene chip comprising (II); (4) a transgenic non-human animal comprising (II); (5) a nucleic acid vector comprising (II); (6) a host cell containing the vector; (7) producing (I); (8) detecting the presence of (I) in a sample, comprising contacting the sample with a detection agent that specifically detects the presence of the peptide in the sample; (9) detecting the presence of (II) in a sample by contacting the sample with an oligonucleotide that hybridizes to (II) under stringent conditions, and determining if the oligonucleotide binds to the nucleic acid molecule in the sample; (10) identifying a modulator of (I) by contacting the peptide with an agent and determining if the agent has modulated the function or activity of the peptide; (11) identifying an agent that binds to (I) by contacting the peptide with an agent and assaying the contacted mixture to determine complex formation with the agent bound to the peptide; (12) a pharmaceutical composition comprising

L99 ANSWER 25 OF 42 BIOTECHDS COPYRIGHT 2002 THOMSON DERWENT AND ISI

ACCESSION NUMBER: 2002-15422 BIOTECHDS

TITLE: New human nuclear hormone receptor proteins and nucleic acids, useful as models or targets for developing human therapeutic targets, and in identifying therapeutic proteins and modulators of nuclear hormone receptor expression; recombinant protein production, transgenic animal and sense and antisense gene use in disease therapy and gene therapy

AUTHOR: WEI M; YE J; YAN C; KETCHUM K A; DI FRANCESCO V; BEASLEY E M

PATENT ASSIGNEE: PE CORP NY

PATENT INFO: WO 2002031146 18 Apr 2002

APPLICATION INFO: WO 2000-US31095 11 Oct 2000

PRIORITY INFO: US 2000-691220 19 Oct 2000

DOCUMENT TYPE: Patent

LANGUAGE: English

OTHER SOURCE: WPI: 2002-426282 [45]

AB DERWENT ABSTRACT: NOVELTY - An isolated peptide (I) comprising/consisting of a fully defined sequence of 457 amino acids (P1) given in the specification, is new. DETAILED DESCRIPTION - An isolated peptide (I) comprising/consisting of: (a) a fully defined sequence of 457 amino acids (P1) given in the specification; (b) an allelic variant/ortholog of P1 encoded by a nucleic acid molecule that hybridizes under stringent conditions to the opposite **strand** of a nucleic acid comprising a sequence of 2086 (S1) or 17000 (S2) base pairs given in the specification; or (c) a fragment of P1 consisting of at least 10 contiguous amino acids, is new. INDEPENDENT CLAIMS are also included for the following: (1) an isolated antibody that selectively binds to (I); (2) an isolated nucleic acid molecule (II) consisting or comprising a sequence which: (a) encodes P1; (b) encodes an allelic variant or ortholog of P1, where the nucleotide sequence hybridizes under stringent conditions to the opposite **strand** of a nucleic acid comprising a sequence of S1 or S2; (c) encodes a fragment of P1 consisting of at least 10 contiguous amino acids; or (d) a complement of (a)-(c); (3) a gene chip comprising (II); (4) a transgenic non-human animal comprising (II); (5) a nucleic acid vector comprising (II); (6) a host cell containing the vector; (7) producing (I) by introducing (II) into a host cell, and culturing the host cell under conditions allowing the expression of the peptide; (8) detecting the presence of (I) in a sample by contacting the sample with a detection agent that specifically detects the peptide, or with an oligonucleotide that hybridizes to the nucleic acid under stringent conditions and determining if the oligonucleotide binds to the nucleic acid in the sample; (9) identifying a modulator of (I) by contacting (I) or a cell expressing (I) with an agent and determining if the agent modulated the function or activity of the peptide; (10) identifying an agent that binds to (I) by contacting the peptide with an agent and assaying the contacted mixture to determine if a complex is formed with the agent bound to the peptide; (11) a pharmaceutical composition comprising the agent identified in (10); (12) treating a disease or condition mediated by a human nuclear hormone receptor protein by administering an agent identified in (10); (13) an isolated human nuclear hormone receptor peptide having an amino acid sequence that is at least 70% homologous with P1; and (14) an isolated nucleic acid encoding a human nuclear hormone receptor peptide, where the nucleic acid shares at least 80% homology with S1 or S2. BIOTECHNOLOGY - Preferred Method: The agent is administered to a host cell comprising an expression vector that expresses the peptide. Preferred Peptide: The human nuclear hormone receptor peptide preferably shares at least 90% homology with P1, and the nucleic acid encoding the peptide preferably shares at least 90% homology with S1 or S2. ACTIVITY - None given. MECHANISM OF ACTION - Gene therapy; Vaccine. USE - The peptides and nucleic acids can be used as models for the development of human therapeutic targets, aid in the identification of therapeutic proteins,

Preparation: (I) is prepared by standard recombinant techniques (claimed). Preferred Molecules: The allelic variants of (I) and (III) preferably share 90% homology with (S2), and (S1) or (S3), respectively. ACTIVITY - None given. MECHANISM OF ACTION - Gene therapy; (I) expression or activity modulator. No supporting data is given. USE - (I) comprising an amino acid sequence of (S2), its allelic variant or ortholog or fragment, is useful for identifying a modulator of a human kinase protein, preferably, the agent is administered to a host cell comprising an expression vector that expresses the peptide. The method optionally involves contacting a cell expressing the peptide with an agent and determining if the agent has modulated the expression of the peptide. (I) comprising an amino acid sequence of (S2), its allelic variant or ortholog or fragment is also useful for identifying an agent that binds to it. (V) is useful for treating a disease or condition mediated by human kinase protein (all claimed). (I) and (III) can be used as models for the development of human therapeutic targets, aid in the identification of therapeutic proteins and serve as targets for the development of human therapeutic agents that modulate kinase protein activity in cells and tissue that express the kinase protein. (I) and (III) can be used as a query sequence to perform a search against sequence databases to, identify other family members or related sequences. (I) is used to raise antibodies or to elicit another immune response, as a reagent in assays designed to quantitatively determine levels of the protein in biological fluids, and as markers for tissues in which the corresponding protein is preferentially expressed. The kinase proteins isolated from humans and their human/mammalian orthologs serve as targets for identifying agents for use in mammalian therapeutic applications, and biological assays related to kinase proteins that are related to members of the protein kinase C subfamily. The proteins can also be used in screening assays to screen a compound for its ability to stimulate or inhibit interaction between kinase protein and a molecule that normally interacts with the kinase protein. The proteins also provide a target for diagnosing a disease or predisposition to disease mediated by the peptide, and in pharmacogenomic analysis. The peptides are also useful for treating a disorder characterized by absence of, inappropriate or unwanted expression of the protein. (II) is useful for isolating (I), purifying (I), and to assess expression of (I) in active stages of a disease, or in an individual with a predisposition towards disease related to the protein's function. The antibodies are also useful for assessing normal and aberrant subcellular localization of cells in various tissues in an organism, in pharmacogenomic analysis, for tissue typing and for inhibiting protein function. (III) is useful as probes, primers, chemical intermediates and in biological assays. The nucleic acid molecules are useful for constructing recombinant vectors, host cells and transgenic animals, and for designing ribozymes. The nucleic acids are also useful in drug screening assays and as a target for treatment by the compounds identified through drug screening. The nucleic acid molecules are also useful for monitoring effectiveness of modulating compounds on the expression or activity of kinase gene in clinical trials or in treatment regimen, and for testing an individual for a genotype that while not necessarily causing the disease nevertheless affects the treatment modality. The nucleic acid molecules are also useful in diagnostic assays for qualitative changes in expression of nucleic acid encoding kinase protein and particularly in qualitative changes that lead to pathology. The nucleic acid molecules can be used to detect mutations in genes encoding kinase proteins and gene expression products such as mRNA. Detection of mutated form of gene encoding kinase associated with a dysfunction provides a diagnostic tool for a active disease or susceptibility to disease which results from overexpression, underexpression or altered expression of kinase protein. (III) also provides vectors for gene therapy in patients with aberrant expression of gene encoding kinase. EXAMPLE - None given. (107 pages)



L99 ANSWER 24 OF 42 BIOTECHDS COPYRIGHT 2002 THOMSON DERWENT AND ISI

ACCESSION NUMBER: 2002-13568 BIOTECHDS

TITLE: Novel human kinase protein, related to protein kinase C subfamily, useful as model for developing human therapeutic targets and serves as target for human therapeutics; recombinant enzyme gene production, antibody, transgenic animal and ribozyme for use in disease therapy and gene therapy

AUTHOR: LI J; GUEGLER K; BEASLEY E M; KETCHUM K A; DI FRANCESCO V

PATENT ASSIGNEE: PE CORP NY

PATENT INFO: WO 2002022795 21 Mar 2002

APPLICATION INFO: WO 2000-US28652 14 Sep 2000

PRIORITY INFO: US 2000-735934 14 Dec 2000

DOCUMENT TYPE: Patent

LANGUAGE: English

OTHER SOURCE: WPI: 2002-393960 [42]

AB DERWENT ABSTRACT: NOVELTY - An isolated human kinase protein (I) that is related to protein kinase C subfamily, consisting or comprising a fully defined sequence of 878 (S2) amino acids as given in the specification, or its fragment comprising 10 contiguous amino acids, or an amino acid sequence of an allelic variant or ortholog of the amino acid sequence of (S2), is new. DETAILED DESCRIPTION - (I) consists or comprises of: an amino acid sequence of (S2); an amino acid sequence of an allelic variant or an ortholog of (S2), where the allelic variant or ortholog is encoded by a nucleic acid molecule that hybridizes under stringent conditions to the opposite **strand** of a nucleic acid molecule having a fully defined sequence of 2637 (S1) (a cDNA molecule) or 43950 (genomic sequence) nucleotides (S3) as given in the specification; a fragment of an amino acid sequence of (S2), comprising 10 contiguous amino acids. The isolated human kinase protein variant has an amino acid sequence that shares 70% homology with (S2). INDEPENDENT CLAIMS are also included for the following: (1) an isolated antibody (II) that selectively binds to (I) comprising the amino acid sequence of (S2), its allelic variant or ortholog, or fragment; (2) an isolated nucleic acid molecule (III) consisting or comprising of a nucleotide sequence that encodes (I) or a nucleotide sequence that is complement of the nucleotide sequence encoding (I), where allelic variant of (III) encoding a human kinase peptide shares at least 80% homology with (S1) or (S3); (3) a gene chip comprising (III) that comprises a nucleotide sequence encoding (I), or its complement; (4) a transgenic non-human animal comprising (III) that comprises a nucleotide sequence encoding (I), or its complement; (5) a nucleic acid vector (IV) comprising (III) that comprises a nucleotide sequence encoding (I), or its complement; (6) a host cell comprising (IV); (7) preparation of (I); (8) detecting the presence of (I) in a sample involves contacting the sample with a detection agent that specifically allows detection of the presence of the peptide in the sample; (9) detecting the presence of (III) in a sample involves contacting the sample with an oligonucleotide that hybridizes to the nucleic acid molecule under stringent conditions and determining whether an oligonucleotide binds to the nucleic acid molecule in the sample; and (10) a pharmaceutical composition (V) comprising an agent that binds to (I), and is identified using (I) (comprising a sequence of (S2), its allelic variant or ortholog or fragment), and a carrier. WIDER DISCLOSURE - The following are also disclosed as new: (1) chimeric or fusion proteins comprising (I); (2) agents identified using screening methods involving (I); (3) non-coding fragments of a nucleic acid molecule having a sequence of (S1) or (S3); (4) kit comprising (II) for detecting (I) comprising an amino acid sequence of (S2), its allelic variant or ortholog or fragment; (5) kits for detecting the presence of nucleic acid encoding kinase protein in a biological sample; (6) analogs or derivatives of (I); and (7) compartmentalized kits comprising necessary reagents for carrying out the above mentioned assays. BIOTECHNOLOGY -

recombinant techniques (claimed). Preferred Molecule: The allelic variants of (I) and (III) preferably share 90% homology with (S2), and (S1) or (S3), respectively. ACTIVITY - None given in the source material. MECHANISM OF ACTION - Gene therapy; (I) expression or activity modulator. No biodata is given in the source material. USE - (I) comprising an amino acid sequence of (S2), its allelic variant or ortholog or fragment, is useful for identifying a modulator of a human transporter protein, preferably, the agent is administered to a host cell comprising an expression vector that expresses the peptide. The method optionally involves contacting a cell expressing the peptide with an agent and determining if the agent has modulated the expression of the peptide. (I) comprising an amino acid sequence of (S2), its allelic variant or ortholog or fragment is also useful for identifying an agent that binds to it. (V) is useful for treating a disease or condition mediated by human transporter protein (all claimed). (I) and (III) can be used as models for the development of human therapeutic targets, aid in the identification of therapeutic proteins and serve as targets for the development of human therapeutic agents that modulate transporter protein activity in cells and tissue that express the transporter protein. (I) and (III) can be used as a query sequence to perform a searches against sequence databases to, identify other family members or related sequences. (I) is used to raise antibodies or to elicit another immune response, as a reagent in assays designed to quantitatively determine levels of the protein in biological fluids, and as markers for tissues in which the corresponding protein is preferentially expressed. The transporter protein isolated from humans and their human/mammalian orthologs serve as targets for identifying agents for use in mammalian therapeutic applications, and biological assays related to transporter protein that are related to members of the zinc transporter subfamily. The proteins can also be used in screening assays to screen a compound for its ability to stimulate or inhibit interaction between transporter protein and a molecule that normally interacts with the transporter protein. The proteins also provide a target for diagnosing a disease or predisposition to disease mediated by the peptide, and in pharmacogenomic analysis. The peptides are also useful for treating a disorders characterized by absence of, inappropriate or unwanted expression of the protein. (II) is useful for isolating (I), purifying (I), and to assess expression of (I) in active stages of a disease, or in an individual with a predisposition towards disease related to the protein's function. The antibodies are also useful for assessing normal and aberrant subcellular localization of cells in various tissues in an organism, in pharmacogenomic analysis, for tissue typing and for inhibiting protein function. (III) is useful as probes, primers, chemical intermediates and in biological assays. The nucleic acid molecules are useful for constructing recombinant vectors, host cells and transgenic animals, and for designing ribozymes. The nucleic acids are also useful in drug screening assays and as a target for treatment by the compounds identified through drug screening. The nucleic acid molecules are also useful for monitoring effectiveness of modulating compounds on the expression or activity of transporter protein gene in clinical trials or in treatment regimen, and for testing an individual for a genotype that while not necessarily causing the disease nevertheless affects the treatment modality. The nucleic acid molecules are also useful in diagnostic assays for qualitative changes in expression of nucleic acid encoding transporter protein and particularly in qualitative changes that lead to pathology. The nucleic acid molecules can be used to detect mutations in genes encoding transporter protein and gene expression products such as mRNA. Detection of mutated form of gene encoding transporter protein associated with a dysfunction provides a diagnostic tool for a active disease or susceptibility to disease which results from over expression, underexpression or altered expression of transporter protein. (III) also provides vectors for gene therapy in patients with aberrant expression of gene encoding transporter protein. (75 pages)

L99 ANSWER 23 OF 42 BIOTECHDS COPYRIGHT 2002 THOMSON DERWENT AND ISI

ACCESSION NUMBER: 2002-14125 BIOTECHDS

TITLE: Novel human transporter proteins, related to zinc transporter subfamily, useful as model for developing human therapeutic targets and serves as target for human therapeutics; vector-mediated gene transfer, expression in host cell and antibody for recombinant protein production, drug screening and gene therapy

AUTHOR: WEI M; KETCHUM K A; DI FRANCESCO V; BEASLEY E M

PATENT ASSIGNEE: PE CORP NY

PATENT INFO: WO 2002024910 28 Mar 2002

APPLICATION INFO: WO 2000-US29218 20 Sep 2000

PRIORITY INFO: US 2000-691219 19 Oct 2000

DOCUMENT TYPE: Patent

LANGUAGE: English

OTHER SOURCE: WPI: 2002-404954 [43]

AB DERWENT ABSTRACT: NOVELTY - An isolated human transporter protein (I) that is related to zinc transporter subfamily, consisting or comprising a fully defined sequence of 372 (S2) amino acids as given in the specification, or its fragment comprising 10 contiguous amino acids, or an amino acid sequence of an allelic variant or ortholog of the amino acid sequence of (S2), is new. DETAILED DESCRIPTION - (I) consists or comprises of: an amino acid sequence of (S2); an amino acid sequence of an allelic variant or an ortholog of (S2), where the allelic variant or ortholog is encoded by a nucleic acid molecule that hybridizes under stringent conditions to the opposite strand of a nucleic acid molecule having a fully defined sequence of 1617 (S1) (a cDNA molecule) or 11101 (genomic sequence) nucleotides (S3) as given in the specification; a fragment of an amino acid sequence of (S2), comprising 10 contiguous amino acids. The isolated human transporter peptide variant has an amino acid sequence that shares 70% homology with (S2). INDEPENDENT CLAIMS are included for the following: (1) an isolated antibody (II) that selectively binds to (I) comprising the amino acid sequence of (S2), its allelic variant or ortholog, or fragment; (2) an isolated nucleic acid molecule (III) consisting or comprising of a nucleotide sequence that encodes (I) or a nucleotide sequence that is complement of the nucleotide sequence encoding (I), where allelic variant of (III) encoding a human transporter peptide shares at least 80% homology with (S1) or (S3); (3) a gene chip comprising (III) that comprises a nucleotide sequence encoding (I), or its complement; (4) a transgenic non-human animal comprising (III) that comprises a nucleotide sequence encoding (I), or its complement; (5) a nucleic acid vector (IV) comprising (III) that comprises a nucleotide sequence encoding (I), or its complement; (6) a host cell comprising (IV); (7) preparation of (I); (8) detecting the presence of (I) in a sample involves contacting the sample with a detection agent that specifically allows detection of the presence of the peptide in the sample; (9) detecting the presence of (III) in a sample involves contacting the sample with an oligonucleotide that hybridizes to the nucleic acid molecule under stringent conditions and determining whether an oligonucleotide binds to the nucleic acid molecule in the sample; and (10) a pharmaceutical composition (V) comprising an agent that binds to (I), and identified using (I) (comprising a sequence of (S2), its allelic variant or ortholog or fragment), and a carrier. WIDER DISCLOSURE - The following are disclosed: (1) chimeric or fusion proteins comprising (I); (2) agents identified using screening methods involving (I); (3) non-coding fragments of a nucleic acid molecule having a sequence of (S1) or (S3); (4) kit comprising (II) for detecting (I) comprising an amino acid sequence of (S2), its allelic variant or ortholog or fragment; (5) kits for detecting the presence of nucleic acid encoding transporter protein in a biological sample; (6) analogs or derivatives of (I); and (7) compartmentalized kits comprising necessary reagents for carrying out the above mentioned assays. BIOTECHNOLOGY - Preparation: (I) is prepared by standard

vector containing the complement of (II) encoding (I) is also useful for treating the above mentioned disorders. (I) or (II) is also useful for inducing immunological response in a mammal. Antibodies which specifically bind to HGPRBMY7 polypeptide can be used for diagnosis or conditions characterized by overexpression of polypeptide or polynucleotide or in assays to monitor patients treated with HGPRBMY7, its agonist or antagonist, and for detecting HGPRBMY7 polypeptide in a sample. HGPRBMY7 polynucleotides are also useful as targets in a **microarray**, to generate hybridization probes. ADMINISTRATION - Pharmaceutical compositions comprising HGPRBMY7 polypeptide, HGPRBMY7 nucleic acids, antibodies to the HGPRBMY7 polypeptide are administered by oral, intravenous, intramuscular, intranasal, enteral route. Dosages range from 0.1-100000 microg. EXAMPLE - G-protein coupled receptor (GPCR) sequences (more than 1300 non-olfactory GPCR sequences available from the GPCRDB database at the European Molecular Biology Laboratory) were used as probes to search the human genomic sequence database. The top genomic exon hits from the BLAST results were searched back against the non-redundant protein and patent sequence databases. From this analysis, exons encoding potential novel GPCRs were identified based on sequence homology. Also the genomic region surrounding the matching exons were analyzed. Based on this analysis, potential full-length sequence of a novel human GPCR, called HGPRBMY7, was identified directly from the genomic sequence. The full-length clone of this GPCR was experimentally obtained by reverse transcriptase (RT)-PCR using the sequence from the genomic data and conventional methods. The complete protein sequence of HGPRBMY7 was analyzed for potential transmembrane domains. The TMPRED program was used for transmembrane prediction. The predicted transmembrane (TM) domains of the HGPRBMY7 match with similar predicted TM domains of related GPCRs at the sequence level. Based on the sequence, structure and known GPCR signature sequences, the orphan protein, HGPRBMY7, was a novel human GPCR. HGPRBMY7 was cloned from a human brain cDNA library by PCR amplification of the predicted cDNA sequence using 5'-GGCCGAATTCGCTGGCAGCTGCCTTTGCAGACTCTAACTCC-3' and 5'-GGCCGAATTCGTCAGCAATATTGATAAGCAGCAGTACAAGTAAATAC-3'. Samples containing human brain cDNA, 5' and 3' oligonucleotides, were subjected to PCR amplification by gel purification of the amplified product. The purified sample was digested with EcoRI, extracted with phenol: chloroform, and ligated into pcDNA6. The resultant plasmids were subjected to DNA sequencing and sequences were verified by comparison with the database sample. Expression profiling of novel human GPCR, HGPRBMY7 was carried out by measuring the steady state levels of mRNA by quantitative PCR, where **strand** cDNA was made from commercially available mRNA. The relative amount of cDNA used in each assay was determined by performing a parallel experiment using a primer pair for the cyclophilin gene, which was expressed in equal amounts in all tissues. The cyclophilin primer pair detected small variations in the amount of cDNA in each sample, and these data were used for normalization of the data obtained with the primer pair of HGPRBMY7. The PCR data were converted into a relative assessment of the difference in transcript abundance among the tissues tested. Transcripts corresponding to the orphan GPCR, HGPRBMY7, were found to be highly expressed in spinal cord. Also, RNA quantification was performed using the Taqman real-time-PCR fluorogenic assay. HGPRBMY7 (also known as GPCR85) messenger RNA was found to be expressed about 60-fold greater in a certain breast cancer cell line, H3396, in comparison to other cancer cell lines in the OCLP-1 (oncology cell line panel). Additionally, HGPRBMY7 was also expressed at moderate levels in a colon carcinoma cell line. Based on HGPRBMY7's expression in the brain, further analysis was carried out to determine if there was any additional specificity within subregions. Transcripts corresponding to HGPRBMY7 were expressed approximately 6 times greater in the thalamus than in the cerebellum. Low level expression was detected in the corpus callosum, caudate nucleus amygdala, and hippocampus. (170 pages)

formulation comprising (I) or (II). BIOTECHNOLOGY - Preparation: (I) is prepared by culturing (VI) under conditions such that the polypeptide is expressed and recovering the polypeptide (claimed). Preferred Polynucleotide: The polynucleotide fragment comprises a nucleotide sequence encoding a G-protein coupled receptor (GPCR) protein, a nucleotide sequence encoding the sequence of (S2) or polypeptide encoded by the cDNA sequence included in (D) which is hybridizable to (S1), or comprises entire nucleotide sequence of (S1) or cDNA sequence included in (D) which is hybridizable to (S1). The nucleotide sequence encoding GPCR protein comprises sequential nucleotide deletions from either the C-terminus or N-terminus. The polynucleotide is localized in thalamus, cerebellum, corpus callosum, caudate nucleus, amygdala, substantia nigra, hippocampus, brain, breast, colon, spinal cord or breast carcinoma cell lines. Preferred Host Cell: (IV) comprises vector sequences. ACTIVITY - Cytostatic; Osteopathic; Antiasthmatic; Antiinflammatory; Hepatotrophic; Antithyroid; Neuroprotective; Antidepressant; Nootropic; Anticonvulsant. MECHANISM OF ACTION - Gene therapy; agonist or antagonist of HGPRBMY7 activity. USE - (I) or (II) is useful for prevention, treating or ameliorating a medical condition. (I) or (II) is also useful for diagnosing a pathological condition or a susceptibility to a pathological condition in a subject which involves determining the presence or absence of mutation in (II) or determining the presence or amount of expression of (I) in a biological sample and diagnosing a pathological condition based on the result. (I) is useful for identifying a binding partner (a peptide) which involves contacting the polypeptide with the binding partner and determining whether the binding partner affects the activity of the polypeptide. (I) is useful for treating a disease, disorder, or a condition related to brain, breast, gastrointestinal or musculo-skeletal systems, such that thalamus-, corpus callosum-, cerebellum-, caudate nucleus-, amygdala-, substantia nigra-, hippocampus-, brain-, breast-, colon-, spinal cord-related disorders are treated. (II) is useful for identifying an activity in a biological assay which involves expressing the HGPRBMY7 sequence of (S2) in a host cell and measuring the resulting activity of the expressed HGPRBMY7. (IV) is useful for identifying a compound that modulates the biological activity of human HGPRBMY7, or a G-protein coupled receptor (GPCR) which involves combining candidate modulator compound with (IV) containing (III), where HGPRBMY7 is expressed by the cell and measuring an effect of the candidate modulator compound on the activity of expressed HGPRBMY7. (VIII) or (IX) is useful for screening candidate compounds capable of modulating activity of GPCR polypeptide which involves contacting test compound with (VII) or (VII), and selecting as candidate modulating compounds those test compounds that modulate activity of the GPCR polypeptide. The candidate compounds are either agonists or antagonists of GPCR activity, and are preferably peptides. The compounds preferably modulate GPCR activity which is associated with thalamus, cerebellum, corpus callosum, caudate nucleus, amygdala, substantia nigra, hippocampus, brain, breast, colon, spinal cord or breast cancer (all claimed). (I) and (II) are useful for diagnosing diseases related to over or underexpression of HGPRBMY7 proteins by identifying mutations in HGPRBMY7 gene using HGPRBMY7 probes or determining HGPRBMY7 protein or mRNA expression levels. (I) and (II) useful for screening, diagnosing, treating or preventing disorders associated with aberrant or uncontrolled cellular growth and/or function such as neoplastic diseases, and disorders related to spinal cord and brain. An antagonist or inhibitor of (I) identified using (I) is useful for treating a neoplastic disorder such as leukemia, myeloma, etc; immunological disorders such as cholecystitis, Grave's disease, osteoarthritis, asthma, neurological disorders such as dementia, depression, Alzheimer's disease, Down's syndrome, epilepsy etc. (I), (II), including agonists or antagonists of the polypeptide are useful for modulating intracellular calcium levels, modulating Ca<sup>2+</sup> sensitive signaling pathways and modulating nuclear factor activator of transcription (NFAT) element associated signaling pathways. An expression

PATENT INFO: WO 2002026823 4 Apr 2002  
APPLICATION INFO: WO 2000-US30351 27 Sep 2000  
PRIORITY INFO: US 2001-315423 28 Aug 2001  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
OTHER SOURCE: WPI: 2002-435195 [46]

AB DERWENT ABSTRACT: NOVELTY - An isolated polypeptide (I) comprising amino acid sequence that is at least 95% identical to polypeptide fragment of a fully defined human G-protein coupled receptor BMY7 (HGPRBMY7) polypeptide sequence of 406 amino acids (S2) as given in specification and having biological activity, polypeptide domain or epitope of (S2), full-length protein of (S2), or variant, allelic variant or species homolog of (S2), is new. DETAILED DESCRIPTION - (I) comprises an amino acid sequence that is at least 90% identical to a polypeptide fragment of (S2), or the encoded sequence included in ATCC deposit number: PTA-2966 (D), and having biological activity; polypeptide domain or epitope of (S2) or encoded sequences included in (D); full-length protein of (S2) or encoded sequence included in (D), or variant, allelic variant, species homolog of (S2); or a polypeptide corresponding to amino acids 2-406 of (S2). INDEPENDENT CLAIMS are included for the following: (1) an isolated nucleic acid molecule (II) consisting of a polynucleotide having a nucleotide sequence of: (i) polynucleotide fragment of a fully defined sequence of 1221 nucleotides (S1) as given in the specification or a polynucleotide fragment of (D) which is hybridizable to (S1); (ii) a polynucleotide encoding polypeptide fragment of, domain of, epitope of (S2) or polypeptide fragment, domain or epitope encoded by (D), which is hybridizable to (S1); (iii) a polynucleotide encoding polypeptide of (S2) or cDNA sequence included in (D) which is hybridizable to (S1), having biological activity; (iv) polynucleotide which is variant or allelic variant of (S1); (v) a polynucleotide encoding a species homolog of (S2); (vi) a polynucleotide which represents the complementary sequence of (S1); (vii) a polynucleotide corresponding to nucleotides 4-1218 or 1-1218 of (S1); or (viii) a polynucleotide capable of hybridizing under stringent conditions to any of the above polynucleotides, where the polynucleotide does not hybridize under stringent conditions to a nucleic acid molecule having a nucleotide sequence of only A residue or of only T residues; (2) a recombinant vector (III) comprising (II); (3) making a recombinant host cell comprising (II); (4) a recombinant host cell (IV) produced using the above method; (5) an isolated antibody (V) that binds specifically to (I); (6) a recombinant host cell (VI) expressing (I); (7) preparation of (I); (8) a polypeptide produced by the above method; (9) a gene corresponding to the cDNA sequence of (S2); (10) a compound (VII) that modulates the biological activity of the HGPRBMY7 as identified using (I), (II) or (IV); (11) a cell (VIII) comprising nuclear factor activator of transcription (NFAT)/cAMP response element (CRE) and (I); and (12) a cell (IX) comprising NFAT G alpha15 and (I). WIDER DISCLOSURE - The following are also disclosed as new: (1) compositions comprising HGPRBMY7 polynucleotide sequence or its fragment, or the encoded HGPRBMY7 polypeptide or its portion; (2) kits for screening and diagnosis of disorders associated with aberrant or uncontrolled cellular development and with the expression of polynucleotide and its encoded polypeptide, comprising (I), (II), nucleotide sequence complementary to (S1), an antibody to HGPRBMY7 polypeptide; (3) compositions for diagnosing spinal cord- and brain-related disorders and response to HGPRBMY7 therapy in humans; (4) diagnostic probes for diseases and a patient's response to therapy; (5) diagnostic kits for determination of nucleotide sequence of human HGPRBMY7 alleles; (6) detecting genetic disposition, susceptibility and response to therapy related to spinal cord and brain; (7) nucleotide sequences that differ from (S1) due to degeneracy of genetic code; (8) recombinant nucleic acid sequences encoding HGPRBMY7 polypeptide operably linked to recombinant nucleic acid sequences encoding fusion protein; (9) polypeptide sequences that intervene between each of the predicted HGPRBMY7 transmembrane domains; and (10) immunological or vaccine

ancestral chromosomes. However, the data so far obtained derive mainly from cytogenetic observations. Cloning and **database** searching of human IT sequences allowed us to identify three classes: (i) short ITs, composed of few, essentially exact T.sub.2AG.sub.3 units; (ii) subtelomeric ITs, composed of larger arrays (several hundred base pairs) including many degenerate units within subtelomeric domains; (iii) fusion ITs, in which two extended stretches of telomeric repeats are oriented head-to-head. The number of short ITs is over 50 and subtelomeric ITs are probably present at all chromosomal ends. Surprisingly, the telomeric sequence in 2q13 remains the only fusion IT so far characterized, and evidence presented here suggests that another member of this class may be present in 1q41. Different molecular mechanisms generated the three classes. In particular, several short ITs interrupt precisely repetitive elements or are flanked by direct repeats of 10-41 bp, and are conserved in gorilla and chimpanzee. These features strongly suggest that telomeric repeats were inserted at intrachromosomal sites through the repair of double-**strand** breaks that occurred in the germline during evolution.

L99 ANSWER 21 OF 42 BIOTECHNO COPYRIGHT 2002 Elsevier Science B.V.  
ACCESSION NUMBER: 1999:29412782 BIOTECHNO  
TITLE: Application of DNA arrays to toxicology  
AUTHOR: Rockett J.C.; Dix D.J.  
CORPORATE SOURCE: J.C. Rockett, Reproductive Toxicol. Div. (MD-72),  
Natl. Hlth. Environm. Effects Res., U.S. EPA, Research  
Triangle Park, NC 27711, United States.  
E-mail: rockett.john@epa.gov  
SOURCE: Environmental Health Perspectives, (1999), 107/8  
(681-685), 15 reference(s)  
CODEN: EVHPAZ ISSN: 0091-6765  
DOCUMENT TYPE: Journal; (Short Survey)  
COUNTRY: United States  
LANGUAGE: English  
SUMMARY LANGUAGE: English

AB DNA array technology makes it possible to rapidly genotype individuals or quantify the expression of thousands of genes on a single filter or glass slide, and holds enormous potential in toxicologic applications. This potential led to a U.S. Environmental Protection Agency-sponsored workshop titled 'Application of **Microarrays** to Toxicology' on 7-8 January 1999 in Research Triangle Park, North Carolina. In addition to providing state-of-the-art information on the application of DNA or gene **microarrays**, the workshop catalyzed the formation of several collaborations, committees, and user's groups throughout the Research Triangle Park area and beyond. Potential application of **microarrays** to toxicologic research and risk assessment include genome-wide expression analyses to identify gene-expression networks and toxicant-specific signatures that can be used to define mode of action, for exposure assessment, and for environmental monitoring. Arrays may also prove useful for monitoring genetic variability and its relationship to toxicant susceptibility in human populations.

L99 ANSWER 22 OF 42 BIOTECHDS COPYRIGHT 2002 THOMSON DERWENT AND ISI  
ACCESSION NUMBER: 2002-15984 BIOTECHDS  
TITLE: Novel human G-protein coupled receptor BMY7 (HGPRBMY7)  
polypeptide, useful for modulators of HGPRBMY7 activity that  
are useful for treating leukemia, cholecystitis, Grave's  
disease, epilepsy, dementia, depression;  
vector-mediated recombinant protein gene transfer and  
expression in host cell for disease or disorder diagnosis,  
prognosis and gene therapy  
AUTHOR: BATTAGLINO P; FEDER J N; MINTIER G; RAMANATHAN C S; WESTPHAL  
R; HAWKEN D R; CACACE A; BARBER L; KORNACKER M G  
PATENT ASSIGNEE: BRISTOL-MYERS SQUIBB CO

COUNTRY: United Kingdom  
LANGUAGE: English  
SUMMARY LANGUAGE: English

AB The DNA **microarray**, a surface that contains an ordered arrangement of each identified open reading frame of a sequenced genome, is the engine of functional genomics. Its output, the expression profile, provides a genome wide snap-shot of the transcriptome. Refined by array-specific statistical instruments and data-mined by clustering algorithms and metabolic pathway **databases**, the expression profile discloses, at the transcriptional level, how the microbe adapts to new conditions of growth - the regulatory networks that govern the adaptive response and the metabolic and biosynthetic pathways that effect the new phenotype. Adaptation to host microenvironments underlies the capacity of infectious agents to persist in and damage host tissues. While monitoring the whole genome transcriptional response of bacterial pathogens within infected tissues has not been achieved, it is likely that the complex, tissue-specific response is but the sum of individual responses of the bacteria to specific physicochemical features that characterize the host milieu. These are amenable to experimentation in vitro and whole-genome expression studies of this kind have defined the transcriptional response to iron starvation, low oxygen, acid pH, quorum-sensing pheromones and reactive oxygen intermediates. These have disclosed new information about even well-studied processes and provide a portrait of the adapting bacterium as a 'system', rather than the product of a few genes or even a few regulons. Amongst the regulated genes that compose this adaptive system are transcription factors. Expression profiling experiments of transcription factor mutants delineate the corresponding regulatory cascade. The genetic basis for pathogenicity can also be studied by using **microarray**-based comparative genomics to characterize and quantify the extent of genetic variability within natural populations at the gene level of resolution. Also identified are differences between pathogen and commensal that point to possible virulence determinants or disclose evolutionary history. The host vigorously engages the pathogen; expression studies using host genome **microarrays** and bacterially infected cell cultures show that the initial host reaction is dominated by the innate immune response. However, within the complex expression profile of the host cell are components mediated by pathogen-specific determinants. In the future, the combined use of bacterial and host **microarrays** to study the same infected tissue will reveal the dialogue between pathogen and host in a gene-by-gene and site- and time-specific manner. Translating this conversation will not be easy and will probably require a combination of powerful bioinformatic tools and traditional experimental approaches - and considerable effort and time.

L99 ANSWER 20 OF 42 BIOTECHNO COPYRIGHT 2002 Elsevier Science B.V.  
ACCESSION NUMBER: 2001:32529711 BIOTECHNO  
TITLE: Human intrachromosomal telomeric-like repeats:  
Sequence organization and mechanisms of origin  
AUTHOR: Azzalin C.M.; Nergadze S.G.; Giulotto E.  
CORPORATE SOURCE: E. Giulotto, Dipart. di Genetica e Microbiologia,  
Adriano Buzzati Traverso, Universita di Pavia, Via  
Abbiategrosso 207, 27100 Pavia, Italy.  
E-mail: giulotto@ipvgen.unipv.it  
SOURCE: Chromosoma, (2001), 110/2 (75-82), 39 reference(s)  
CODEN: CHROAU ISSN: 0009-5915  
DOCUMENT TYPE: Journal; Article  
COUNTRY: Germany, Federal Republic of  
LANGUAGE: English  
SUMMARY LANGUAGE: English  
AB The intrachromosomal location of (T.sub.2AG.sub.3).sub.n telomeric sequences has been reported in several species. It was proposed that interstitial telomeres (ITs) originated through telomeric fusion of



expression. Various cloning and cDNA **microarray** strategies are being used to determine the complete spectrum of gene expression changes underlying these alterations in human melanoma cells. An efficient approach, Rapid Subtraction Hybridization (RaSH), has been developed that is permitting the identification of genes of potential relevance to cancer growth control and terminal cell differentiation. RaSH cDNA libraries are prepared from double-**stranded** cDNAs that are enzymatically digested into small fragments, ligated to adapters, and PCR amplified followed by incubation of tester and driver PCR fragments. This subtraction hybridization scheme is technically simple and results in the identification of a high proportion of differentially expressed sequences, including known genes and those not described in current DNA **databases**. The RaSH approach represents an efficient methodology for identifying and cloning genes displaying differential expression that associate with and potentially regulate complex biological processes.

L99 ANSWER 18 OF 42 BIOTECHNO COPYRIGHT 2002 Elsevier Science B.V.  
ACCESSION NUMBER: 2002:34309149 BIOTECHNO  
TITLE: Expression pattern of lung cancer related genes in malignant transformation of BEP2D  
AUTHOR: Fan B.-X.; Zhang K.-T.; Li G.; Xie L.; Ma S.-H.; Ge S.-L.; Xiang X.-Q.; Hu Y.-C.; Wang S.-Q.; Zhou P.-K.; Wu D.-C.  
CORPORATE SOURCE: K.-T. Zhang, Department of Molecular Toxicology, Beijing Inst. of Radiation Medicine, Beijing 100850, China.  
SOURCE: E-mail: zhangkt@nic.bmi.ac.cn  
Chinese Journal of Cancer Research, (2002), 14/1 (18-23), 15 reference(s)  
CODEN: CJCRFH ISSN: 1000-9604  
DOCUMENT TYPE: Journal; Article  
COUNTRY: China  
LANGUAGE: English  
SUMMARY LANGUAGE: English  
AB Objective: To detect the expression difference of 60 lung cancer associated genes in human bronchial epithelial malignant transformation cell model (BEP2D) induced by alpha-particles. Methods: 60 lung cancer associated genes were collected and micro-arrayed onto the microscope slides using **Cartesian PixSys5500 cDNA Microarray** machine. Total RNA from BEP2D cells and passage 20 (R15H-20), passage 35 (R15H-35) cells derived from BEP2D following 1.5 Gy alpha-particles was extracted and labeled by fluorescent dye. The labeled probe was then hybridized with the cDNA. Results: 40, 47, 20 genes were detected in BEP2D, R15H-20 and R15H-35 respectively. The expression level of tumor suppressor genes decreased greatly in the transformed R15H-35. Most oncogenes decreased slightly in R15H-20. Most growth factors expressed only in R15H-20. Conclusion: In human bronchial epithelial malignant transformed cell model generated by alpha-particles, the loss-function of tumor suppressor genes at initiation stage was dominant, some related oncogenes and growth factors promoted the malignant transformation.

L99 ANSWER 19 OF 42 BIOTECHNO COPYRIGHT 2002 Elsevier Science B.V.  
ACCESSION NUMBER: 2002:34602239 BIOTECHNO  
TITLE: **Microarray** analysis of bacterial pathogenicity  
AUTHOR: Schoolnik G.K.  
CORPORATE SOURCE: G.K. Schoolnik, Department of Medicine, Stanford University Medical School, Stanford, CA 94305, United States.  
SOURCE: Advances in Microbial Physiology, (2002), 46/- (1-45), 65 reference(s)  
CODEN: AMIPB2 ISSN: 0065-2911  
DOCUMENT TYPE: Journal; General Review

SOURCE: NH, 03431: jtonk@s-and-s.com USA  
Analytical Biochemistry, (August 15, 2001) Vol. 295, No. 2,  
pp. 149-157. print.  
ISSN: 0003-2697.

DOCUMENT TYPE: Article  
LANGUAGE: English  
SUMMARY LANGUAGE: English

AB Expression **microarrays** are often constructed by the immobilization of PCR products on two-dimensional modified glass slides or on three-dimensional microporous substrates. In this study we investigate whether the length of the immobilized species and the substrate choice influence hybridization dynamics. Using a simple bimolecular mass action controlled model to describe hybridization, we observed that the extent of hybridization and the initial velocities were directly dependent on the length of the immobilized species. An inflection point was noted at a length of 712 bases, above which the influence of length on hybridization rate decreased. Interestingly, we observed no differences in these parameters whether hybridization occurred on a two- or three-dimensional surface. Furthermore, the affinity of the solution phase labeled species for the immobilized species was identical for all arrayed lengths on both surfaces. These data indicate a similar interaction of the noncovalently immobilized species with either surface. Finally, we have determined that competitive hybridization on expression **microarrays** is nonlinear with respect to time and concentration of competitor. This observation is critical for analysis of expression array data.

L99 ANSWER 16 OF 42 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

ACCESSION NUMBER: 2001:355526 BIOSIS  
DOCUMENT NUMBER: PREV200100355526  
TITLE: **Microarray** tools, kits, reagents, and services.  
AUTHOR(S): Martinsky, Todd (1); Haje, Paul  
CORPORATE SOURCE: (1) TeleChem International, Inc., Sunnyvale, CA USA  
SOURCE: Schena, Mark. (2000) pp. 201-220. Microarray biochip technology. print.  
Publisher: Eaton Publishing 154 E. Central Street, Natick, MA, 01760, USA.  
ISBN: 1-881299-37-6 (cloth).

DOCUMENT TYPE: Book  
LANGUAGE: English  
SUMMARY LANGUAGE: English

L99 ANSWER 17 OF 42 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

ACCESSION NUMBER: 2001:7249 BIOSIS  
DOCUMENT NUMBER: PREV200100007249  
TITLE: RaSH, a rapid subtraction hybridization approach for identifying and cloning differentially expressed genes.  
AUTHOR(S): Jiang, Hongping; Kang, Dong-chul; Alexandre, Deborah; Fisher, Paul B. (1)  
CORPORATE SOURCE: (1) Departments of Pathology and Urology, College of Physicians and Surgeon, Columbia University, 630 West 168th Street, BB-15-1501, New York, NY, 10032: pbf1@columbia.edu USA  
SOURCE: Proceedings of the National Academy of Sciences of the United States of America, (November 7, 2000) Vol. 97, No. 23, pp. 12684-12689. print.  
ISSN: 0027-8424.

DOCUMENT TYPE: Article  
LANGUAGE: English  
SUMMARY LANGUAGE: English

AB Human melanoma cells growth-arrest irreversibly and terminally differentiate on treatment with a combination of fibroblast interferon and the protein kinase C activator mezerein. This experimental protocol also results in a loss of tumorigenic potential and profound changes in gene

strains, will also be produced soon by recombinant organisms having de novo engineered biosynthetic pathway enzyme systems. The biomolecular engineering era is here, and many of benefits will be derived from this field of scientific research for years to come if we are willing to put it to good use.

L99 ANSWER 14 OF 42 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

ACCESSION NUMBER: 2001:263972 BIOSIS

DOCUMENT NUMBER: PREV200100263972

TITLE: Development of human brain cDNA **microarray** to understand the mechanism(s) of action of toxin.

AUTHOR(S): Mohamed, A. Jamal (1); Emmanuel Selvanayagam, Z. (1); Srinivasan, K. N. (1); Cabrera, J. F.; Lay Pheng, T. (1); Khadijah, S. (1); Siew Peng, T. (1); Gopalakrishnakone, P. (1)

CORPORATE SOURCE: (1) National University of Singapore, DNA Microarray Lab, Dept of Anatomy, 117597, Singapore Singapore

SOURCE: FASEB Journal, (March 7, 2001) Vol. 15, No. 4, pp. A381. print.

Meeting Info.: Annual Meeting of the Federation of American Societies for Experimental Biology on Experimental Biology 2001 Orlando, Florida, USA March 31-April 04, 2001  
ISSN: 0892-6638.

DOCUMENT TYPE: Conference

LANGUAGE: English

SUMMARY LANGUAGE: English

AB We fabricated cDNA **microarray** to identify genes responsive to toxin and also to explicate the putative mechanism(s) of toxin action. **Microarray** containing 1864 human brain cDNAs of unknown function were arrayed on poly-L-lysine coated glass slides. A high speed robotic Microarrayer (**Cartesian Technologies Inc.**, USA) was used to print a batch of 30 slides using five printing pins, with a cDNA spot diameter size of 100µm and 250µm spacing between cDNA spots. We used this **microarray** to study the mechanism(s) of action of scorpion toxin in human brain cell line. HTB cells, a human cell line isolated from explant cultures of glioma, were cultured and exposed to HfTx1, a peptide toxin purified from the venom of the scorpion, *Heterometrus fulvipes*. Fluorescent cDNA probes were prepared from total RNA isolated from normal and scorpion toxin (HfTx1) exposed HTB cell lines in single-round reverse transcription reaction in the presence of Cy3-dUTP and Cy5-dUTP respectively. The two cDNA probes were mixed, purified and simultaneously hybridized to the human brain cDNA chip at 62degreeC for 12 hrs. After stringent washing, hybridized DNA on arrays were scanned using laser activated confocal scanner. Average signal intensity and local background measurements were obtained/analyzed for each spot on the array by image analysis software (Quantarray, GSI Lumonics, USA). The color images of the hybridization results were made by representing the Cy3 fluorescent image as green and the Cy5 image as red and superimposing the two color images. Comparative expression analysis of scorpion toxin treated versus control cell lines in our **microarray** hybridization experiments revealed different cDNA clones that displayed fluorescent ratios of greater than 2.0 fold. cDNA corresponding to each of the interesting array elements were sequenced, searched in database and identified few genes, responsive to HfTx1 toxin, which are involved in the ion channels.

L99 ANSWER 15 OF 42 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

ACCESSION NUMBER: 2001:433988 BIOSIS

DOCUMENT NUMBER: PREV200100433988

TITLE: Expression **microarray** hybridization kinetics depend on length of the immobilized DNA but are independent of immobilization substrate.

AUTHOR(S): Stillman, Brett A.; Tonkinson, John L. (1)

CORPORATE SOURCE: (1) Schleicher and Schuell, Inc., 10 Optical Avenue, Keene,

4

ACCESSION NUMBER: 2000:123232 BIOSIS  
DOCUMENT NUMBER: PREV200000123232  
TITLE: Recent progress in biomolecular engineering.  
AUTHOR(S): Ryu, Dewey D. Y. (1); Nam, Doo-Hyun  
CORPORATE SOURCE: (1) Biochemical Engineering Program, University of  
California, Davis, CA, 95616 USA  
SOURCE: Biotechnology Progress, (Jan. Feb., 2000) Vol. 16, No. 1,  
pp. 2-16.  
ISSN: 8756-7938.  
DOCUMENT TYPE: General Review  
LANGUAGE: English  
SUMMARY LANGUAGE: English

AB During the next decade or so, there will be significant and impressive advances in biomolecular engineering, especially in our understanding of the biological roles of various biomolecules inside the cell. The advances in high throughput screening technology for discovery of target molecules and the accumulation of functional genomics and proteomics data at accelerating rates will enable us to design and discover novel biomolecules and proteins on a rational basis in diverse areas of pharmaceutical, agricultural, industrial, and environmental applications. As an applied molecular evolution technology, DNA shuffling will play a key role in biomolecular engineering. In contrast to the point mutation techniques, DNA shuffling exchanges large functional domains of sequences to search for the best candidate molecule, thus mimicking and accelerating the process of sexual recombination in the evolution of life. The phage-display system of combinatorial peptide libraries will be extensively exploited to design and create many novel proteins, as a result of the relative ease of screening and identifying desirable proteins. Even though this system has so far been employed mainly in screening the combinatorial antibody libraries, its application will be extended further into the science of protein-receptor or protein-ligand interactions. The bioinformatics for genome and proteome analyses will contribute substantially toward ever more accelerated advances in the pharmaceutical industry. Biomolecular engineering will no doubt become one of the most important scientific disciplines, because it will enable systematic and comprehensive analyses of gene expression patterns in both normal and diseased cells, as well as the discovery of many new high-value molecules. When the functional genomics **database**, EST and SAGE techniques, **microarray** technique, and proteome analysis by 2-dimensional gel electrophoresis or capillary electrophoresis in combination with mass spectrometer are all put to good use, biomolecular engineering research will yield new drug discoveries, improved therapies, and significantly improved or new bioprocess technology. With the advances in biomolecular engineering, the rate of finding new high-value peptides or proteins, including antibodies, vaccines, enzymes, and therapeutic peptides, will continue to accelerate. The targets for the rational design of biomolecules will be broad, diverse, and complex, but many application goals can be achieved through the expansion of knowledge based on biomolecules and their roles and functions in cells and tissues. Some engineered biomolecules, including humanized Mab's, have already entered the clinical trials for therapeutic uses. Early results of the trials and their efficacy are positive and encouraging. Among them, Herceptin, a humanized Mab for breast cancer treatment, became the first drug designed by a biomolecular engineering approach and was approved by the FDA. Soon, new therapeutic drugs and high-value biomolecules will be designed and produced by biomolecular engineering for the treatment or prevention of not-so-easily cured diseases such as cancers, genetic diseases, age-related diseases, and other metabolic diseases. Many more industrial enzymes, which will be engineered to confer desirable properties for the process improvement and manufacturing of high-value biomolecular products at a lower production cost, are also anticipated. New metabolites, including novel **antibiotics** that are active against resistant

CORPORATE SOURCE: (1) Biochemical Engineering Program, Department of Chemical Engineering and Material Science, University of California, One Shields Avenue, Davis, CA, 95616 USA

SOURCE: Journal of Molecular Catalysis B Enzymatic, (4 September, 2000) Vol. 10, No. 1-3, pp. 23-37. print.  
ISSN: 1381-1177.

DOCUMENT TYPE: General Review

LANGUAGE: English

SUMMARY LANGUAGE: English

AB The advances in high throughput screening technology for discovery of target molecules and the accumulation of functional genomics and proteomics data at an ever-accelerating rate will enable us to design and discover novel biomolecules and proteins on a rational basis in diverse areas of pharmaceutical, agricultural, industrial, and environmental applications. The biomolecular engineering will no doubt become one of the most important scientific disciplines in that it will enable us to comprehensively analyze gene expression patterns in both normal and diseased cells and to discover many new biologically active molecules rationally and systematically. As an applied molecular evolution technology, DNA shuffling will play a key role in biomolecular engineering. In contrast to the point mutation techniques, DNA shuffling exchanges large functional domains of sequences to search for the best candidate molecule, thus mimicking and accelerating the process of sexual recombination in the evolution of life. The phage-display system of combinatorial peptide libraries will be extensively exploited to design and create many more novel proteins, due to the relative ease of screening and identifying desirable proteins. Its application will be extended further into the science of protein-receptor or protein-ligand interactions. The bioinformatics including EST-based or SAGE-tag-based functional genomics and proteomics will continue to advance rapidly. Its biological knowledge base will expand the scope of biomolecular engineering, and the impact of well-coordinated biomolecular engineering research will be very significant on our understanding of gene expression, upregulation and downregulation, and posttranslational protein processing in healthy and diseased cells. The bioinformatics for genome and proteome analysis will contribute substantially toward ever more accelerated advances in pharmaceutical industry. When the functional genomics **database**, EST and SAGE techniques, **microarray** technique, and proteome analysis by 2-dimensional gel electrophoresis or capillary electrophoresis are all put to good use, the biomolecular engineering research will yield new drug discoveries, improved therapies, and new or significantly improved bioprocesses. With the advances in biomolecular engineering, the rate of finding new high-value peptides or proteins including antibodies, vaccines, enzymes, and therapeutic peptides will continue to be accelerated. The targets for rational design of biomolecules will be very broad, diverse, and complex, but many application goals can be achieved through the expansion of knowledge base on biomolecules of interest and their roles and functions in cells and tissues. In the near future, more therapeutic drugs and high-value biomolecules will be designed and produced for the treatment or prevention of not-so-easily-cured diseases such as cancers, genetic diseases, age-related diseases, and other metabolic diseases. Also anticipated are many more industrial enzymes that will be engineered to confer desirable properties for the process improvement and manufacturing of many high-value biomolecular products. Many more new metabolites including novel **antibiotics** that are active against resistant strains will be also produced by recombinant organisms having de novo engineered biosynthetic pathway enzyme systems. The biomolecular engineering era is here and a great deal of benefits can be derived from this field of scientific research for many years to come if we are willing to put it to good use.

amplification was probably due to the unique properties of the microelectronic chip design. The anchored SDA allowed complete sepn. of amplification primers while maintaining an open format. PCR is an efficient means in which to amplify target DNA, but adapting PCR to an anchored format is difficult due to the high temp. and cycling requirements. The advantage of anchored SDA over PCR amplification strategies is the elimination of the requirement for continual bridging of anchored amplicon and amplification primer. The use of anchored SDA with microelectronic chips provided a convenient design and development platform for many nucleic acid-based assays. The anchored SDA had the potential of streamlining any nucleic-acid based diagnostic assay by allowing amplification and detection to occur on the same platform. It can also enhance the capability of miniaturized instruments to conduct on site testing by allowing efficient multiplexed amplification reactions.

REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L99 ANSWER 11 OF 42 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE  
2

ACCESSION NUMBER: 2000:166847 BIOSIS

DOCUMENT NUMBER: PREV200000166847

TITLE: In vitro cloning of complex mixtures of DNA on microbeads: Physical separation of differentially expressed cDNAs.

AUTHOR(S): Brenner, Sydney; Williams, Steven R.; Vermaas, Eric H.; Storck, Thorsten; Moon, Keith; McCollum, Christie; Mao, Jen-I; Luo, Shujun; Kirchner, James J.; Eletr, Sam; DuBridge, Robert B.; Burcham, Timothy; Albrecht, Glenn (1)

CORPORATE SOURCE: (1) Lynx Therapeutics, Inc., 25861 Industrial Boulevard, Hayward, CA, 94545 USA

SOURCE: Proceedings of the National Academy of Sciences of the United States of America., (Feb. 15, 2000) Vol. 97, No. 4, pp. 1665-1670.  
ISSN: 0027-8424.

DOCUMENT TYPE: Article

LANGUAGE: English

SUMMARY LANGUAGE: English

AB We describe a method for cloning nucleic acid molecules onto the surfaces of 5- $\mu$ m microbeads rather than in biological hosts. A unique tag sequence is attached to each molecule, and the tagged library is amplified. Unique tagging of the molecules is achieved by sampling a small fraction (1%) of a very large repertoire of tag sequences. The resulting library is hybridized to microbeads that each carry approx 10<sup>6</sup> **strands** complementary to one of the tags. About 10<sup>5</sup> copies of each molecule are collected on each microbead. Because such clones are segregated on microbeads, they can be operated on simultaneously and then assayed separately. To demonstrate the utility of this approach, we show how to label and extract microbeads bearing clones differentially expressed between two libraries by using a fluorescence-activated cell sorter (FACS). Because no prior information about the cloned molecules is required, this process is obviously useful where sequence **databases** are incomplete or nonexistent. More importantly, the process also permits the isolation of clones that are expressed only in given tissues or that are differentially expressed between normal and diseased states. Such clones then may be spotted on much more cost-effective, tissue- or disease-directed, low-density planar **microarrays**.

L99 ANSWER 12 OF 42 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE  
3

ACCESSION NUMBER: 2000:453061 BIOSIS

DOCUMENT NUMBER: PREV200000453061

TITLE: Biomolecular engineering: A new frontier in biotechnology.

AUTHOR(S): Ryu, Dewey D. Y. (1); Nam, Doo-Hyun

DOCUMENT NUMBER: 134:37908  
TITLE: Non-cognate hybridization system (NCHS) to probe  
non-cognate nucleic acid sequences for use in  
diagnosis  
INVENTOR(S): Schrenzel, Jacques; Hibbs, Jonathan  
PATENT ASSIGNEE(S): Switz.  
SOURCE: PCT Int. Appl., 58 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000075377	A2	20001214	WO 2000-US15893	20000602
WO 2000075377	A3	20010517		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR,  
CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU,  
ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU,  
LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD,  
SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA,  
ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM  
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,  
DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ,  
CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 1999-137327P P 19990603

AB The present invention comprises a non-cognate hybridization system (NCHS). The NCHS generally includes a hybridization technol. that is simply and economically used to probe for non-cognate nucleic acid sequences, i.e., for nucleic acid **strands** without known target sequences. NCHS causes nucleic acids, bound to a probe surface, to create a hybridization pattern that provides information about the presence and/or quantity of the nucleic acid sequences in a sample. The NCHS results normally orient the examiner towards a small no. of specific diagnoses across a wide variety of diagnostic categories (including but not limited to infections, neoplasms and autoimmune diseases). The test will also identify final-common-pathway syndromes such as sepsis, anaphylaxis and tumor necrosis. While the test utilizes genetic information, it does not depend on prior knowledge of the genes involved in a particular disease or syndrome.

L99 ANSWER 10 OF 42 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2001:752118 CAPLUS  
DOCUMENT NUMBER: 136:50499  
TITLE: **Antimicrobial** resistance and bacterial  
identification utilizing a microelectronic chip array  
AUTHOR(S): Westin, Lorelei; Miller, Carolyn; O'Connell, James P.  
CORPORATE SOURCE: Departments of Advanced Research, Nanogen, Inc., San  
Diego, CA, USA  
SOURCE: Proceedings - Water Quality Technology Conference  
(2000) 58-75  
CODEN: PWQCD2; ISSN: 0164-0755  
PUBLISHER: American Water Works Association  
DOCUMENT TYPE: Journal; (computer optical disk)  
LANGUAGE: English

AB A novel in situ amplification assay, anchored SDA, which simultaneously multiplex amplifies ten different DNA targets, was described. The reliance of this new technol. on the proprietary microelectronic chip array for amplification and identification of genomic bacterial DNA target was evaluated. Anchored SDA used a solid substrate, creating micro-amplification zones where individual reactions compete only for the availability of reagents. The success of anchored SDA multiplex

L99 ANSWER 7 OF 42 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2001:625382 CAPLUS  
DOCUMENT NUMBER: 136:322694  
TITLE: Study on differentially expressed genes in postburn hypertrophic scar by cDNA **microarray**  
AUTHOR(S): Ma, Bing; Wu, Jun; Yi, Shaoxuan; Luo, Gaoxing; He, Weifeng; Wang, Zhenxiang; Chen, Xiwei  
CORPORATE SOURCE: Research Institute of Burns, Southwest Hospital, Third Military Medical University, Chungking, 400038, Peop. Rep. China  
SOURCE: Zhonghua Chuangshang Zazhi (2001), 17(6), 334-337  
CODEN: ZCZAFD; ISSN: 1001-8050  
PUBLISHER: Zhonghua Chuangshang Zazhi Bianjibu  
DOCUMENT TYPE: Journal  
LANGUAGE: Chinese

AB The differently expressed genes between postburn hypertrophic scar and normal skin tissue were screened by cDNA microarray. The total RNAs from 3 cases were isolated from the tissues and purified to mRNAs by oligotex. The PCR products of 4096 genes were spotted onto a chem. substance-coated glass plate in array using **Cartesian** Pixsys 7500. DNA was fixed onto the glass plate after series of treatments. Both mRNAs from the postburn hypertrophic scar and normal skin tissue were reversely transcribed to cDNAs with the incorporation of fluorescent dUTP to prep. the hybridization probes. The mixed probes were hybridized to the cDNA microarray. After high-stringent washing, the cDNA microarray scanned for the fluorescent signals and showed differences between 2 tissues. Among 4096 target genes, the expression level of 128 genes differed in 3 cases between the postburn hypertrophic scar and normal skin tissue. Genes including the apoptotic genes, immune related genes, cellular signal and transferring genes take part in the development of postburn hypertrophic scar.

L99 ANSWER 8 OF 42 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2001:571650 CAPLUS  
DOCUMENT NUMBER: 136:242237  
TITLE: Functional genomics of *Caenorhabditis elegans*  
AUTHOR(S): Sugimoto, Asako  
CORPORATE SOURCE: Graduate School of Science, Department of Biochemistry, University of Tokyo, Japan  
SOURCE: Posutoshikuensu no Genomu Kagaku (2001), Volume 4, 16-29. Editor(s): Sakaki, Yoshiyuki; Kohara, Yuji. Nakayama Shoten: Tokyo, Japan.  
CODEN: 69AWVM  
DOCUMENT TYPE: Conference; General Review  
LANGUAGE: Japanese

AB A review. Recent progress of functional genomics on *Caenorhabditis elegans* is reviewed. In addn. to the information on the resources of *C. elegans* cDNA clones and EST for them, technologies such as DNA microarray and whole mount in situ hybridization were described as important tools for gene expression profiling of *C. elegans*. Some details of the RNA interference (RNAi) technol. using double **strand** RNAs homologous to the target genes were also presented as an effective gene silencing strategy in clarifying gene function. For silencing the genes assocd. with neural system to which RNAi were known to be ineffective, the development of the method for systematic prodn. of *C. elegans* mutant was also discussed. Studies on protein-protein interaction that used *C. elegans* as a test case were also described with the concepts of interlog and IST clustering for evaluation of biol. significance of the protein interaction. Information on available **databases** on *C. elegans* genomics were also summarized with web-site information.

L99 ANSWER 9 OF 42 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2000:881362 CAPLUS



## PRIORITY APPLN. INFO.:

US 1999-165398P P 19991105

US 2000-196571P P 20000411

AB The invention discloses methods, gene **databases**, gene arrays, protein arrays, and devices that may be used to det. the hypersensitivity of individuals to a given agent, such as drug or other chem., in order to prevent toxic side effects. In one embodiment, methods of identifying hypersensitivity in a subject by obtaining a gene expression profile of multiple genes assocd. with hypersensitivity of the subject suspected to be hypersensitive, and identifying in the gene expression profile of the subject a pattern of gene expression of the genes assocd. with hypersensitivity are disclosed. The gene expression profile of the subject may be compared with the gene expression profile of a normal individual and a hypersensitive individual. The gene expression profile of the subject that is obtained may comprise a profile of levels of mRNA or cDNA. The gene expression profile may be obtained by using an array of nucleic acid probes for the plurality of genes assocd. with hypersensitivity. The expression of the genes predetd. to be assocd. with hypersensitivity is directly related to prevention or repair of toxic damage at the tissue, organ or system level. Gene **databases** arrays and app. useful for identifying hypersensitivity in a subject are also disclosed.

L99 ANSWER 6 OF 42 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2001:101413 CAPLUS

DOCUMENT NUMBER: 134:128203

TITLE: **Microarrays** and their manufacture

INVENTOR(S): Anderson, Norman G.; Anderson, N. Leigh; Braatz, James A.

PATENT ASSIGNEE(S): Large Scale Proteomics, Corp., USA

SOURCE: PCT Int. Appl., 103 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 3

## PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001009607	A1	20010208	WO 2000-US20695	20000728
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
EP 1204867	A1	20020515	EP 2000-955276	20000728
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL			
US 2001041339	A1	20011115	US 2001-880019	20010614

## PRIORITY APPLN. INFO.:

US 1999-146653P P 19990730

US 2000-482460 A 20000113

WO 2000-US20695 W 20000728

AB The instant invention relates to micro arrays contg. bioreactive mols., uses thereby, and methods for manuf. thereof. The arrays are constructed by sectioning **bundles** of tubules or rods, each contg. unique reactants to produce large nos. of identical arrays.

REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001094611	A2	20011213	WO 2001-US18424	20010607
WO 2001094611	A3	20020418		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
AU 2001075349	A5	20011217	AU 2001-75349	20010607
PRIORITY APPLN. INFO.:			US 2000-209778P P	20000607
			WO 2001-US18424 W	20010607

AB Method and system to predict and optimize probe-target hybridization are provided. The method may be implemented using six interactive, interrelated, software modules. Module 1 predicts the hybridization thermodyn. of a duplex given the two **strands**. Module 2 finds the best primer of a given length binding to a given target. Module 3 executes a primer walk to find alternative binding sites of a given primer on a given target. Module 5 is a combination of Modules 2 and 3. Module 6 finds the alternative binding sites of a given primer on a given target (Module 3) and calcs. the concn. of target with primer bound at primary and alternative sites. Module 7 is a combination of Modules 2 and 5 and also calcs. the various concns. The six modules can be operated either through an interactive user interface or using batch file submission as provided by Module 4. The program is suited to predict DNA/DNA, RNA/RNA, and RNA/DNA systems.

L99 ANSWER 5 OF 42 CAPLUS COPYRIGHT 2002 ACS  
ACCESSION NUMBER: 2001:338762 CAPLUS  
DOCUMENT NUMBER: 134:362292  
TITLE: Methods of determining individual hypersensitivity to a pharmaceutical agent from gene expression profile  
INVENTOR(S): Farr, Spencer  
PATENT ASSIGNEE(S): Phase-1 Molecular Toxicology, USA  
SOURCE: PCT Int. Appl., 222 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001032928	A2	20010510	WO 2000-US30474	20001103
WO 2001032928	A3	20020725		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			

UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU,  
TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH,  
CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR,  
BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

DE 10104937 A1 20020814 DE 2001-10104937 20010129

PRIORITY APPLN. INFO.: DE 2001-10104937 A 20010129

AB The Invention discloses a method for the anal. of the methylation of specific cytosine bases in genomic DNA samples, characterized by the fact that the following steps are implemented: (a) the genomic DNA is chem. treated in such a manner that cytosine is converted into uracil or a similar acting base regarding the base pairing behavior in the DNA duplex, 5-methylcytosine however remains basically unmodified; (b) the chem. treated DNA is amplified using at least one oligonucleotide (type A) as primer in a polymerase reaction, whereby the two **strands** of the polymerase reaction product are manufd. in unequal quantities; (c) the amplificate is hybridized with one or more pairs of oligonucleotides (type B), which hybridize to the positions which are to be examd. regarding their methylation status in the genomic DNA sample whereby one oligonucleotide of each pair hybridizes preferentially in each case if in the genomic DNA sample the position was methylated, while the other oligonucleotide of the pair hybridizes preferentially, if the position was unmethylated. Each oligonucleotide of a pair is labeled with a unique fluorescent label; (d) the fluorescence polarization characteristics of the soln. are measured, whereby for each fluorescent label used one dets. the degree of polarization.

L99 ANSWER 3 OF 42 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2002:696648 CAPLUS

DOCUMENT NUMBER: 137:229908

TITLE: Protein and cDNA sequences of human  
n-acetyltransferase-2 (NAT-2) variants and its  
therapeutic uses

INVENTOR(S): Thomann, Hans-Ulrich; Wall, Kristen; Fitzgerald,  
Michael

PATENT ASSIGNEE(S): USA

SOURCE: U.S. Pat. Appl. Publ., 25 pp.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002128215	A1	20020912	US 2001-776407	20010202

PRIORITY APPLN. INFO.: US 2000-179876P P 20000202

AB The invention relates to cDNA and protein sequences of human n-acetyltransferase-2. This invention relates to novel polymorphisms of the human NAT-2 gene which can be involved in drug metab. and various disorders. The present invention further relates to polymorphisms as they exist within the general population and within various racial groups.

L99 ANSWER 4 OF 42 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2001:904563 CAPLUS

DOCUMENT NUMBER: 136:17715

TITLE: Method and system for predicting nucleic acid  
hybridization thermodynamics and computer-readable  
storage medium for use therein

INVENTOR(S): Santalucia, John, Jr.; Peyret, Nicolas

PATENT ASSIGNEE(S): Wayne State University, USA

SOURCE: PCT Int. Appl., 100 pp.

CODEN: PIXXD2

L99 ANSWER 1 OF 42 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 1  
ACCESSION NUMBER: 2001:223983 CAPLUS  
DOCUMENT NUMBER: 135:164368  
TITLE: **Antimicrobial** resistance and bacterial  
identification utilizing a microelectronic chip array  
AUTHOR(S): Westin, Lorelei; Miller, Carolyn; Vollmer, Dana;  
Canter, David; Radtkey, Ray; Nerenberg, Michael;  
O'Connell, James P.  
CORPORATE SOURCE: Department of Advanced Research, Nanogen, Inc., San  
Diego, CA, 92121, USA  
SOURCE: Journal of Clinical Microbiology (2001), 39(3),  
1097-1104  
CODEN: JCMIDW; ISSN: 0095-1137  
PUBLISHER: American Society for Microbiology  
DOCUMENT TYPE: Journal  
LANGUAGE: English  
AB Species-specific bacterial identification of clin. specimens is often  
limited to a few species due to the difficulty of performing multiplex  
reactions. In addn., discrimination of amplicons is time-consuming and  
laborious, consisting of gel electrophoresis, probe hybridization, or  
sequencing technol. To simplify the process of bacterial identification,  
the authors combined anchored in situ amplification on a microelectronic  
chip array with discrimination and detection on the same platform. Here,  
the authors describe the simultaneous amplification and discrimination of  
6 gene sequences which are representative of different bacterial  
identification assays: Escherichia coli gyrA, Salmonella gyrA,  
Campylobacter gyrA, E. coli parC, Staphylococcus mecA, and Chlamydia  
cryptic plasmid. The assay can detect both plasmid and transposon genes  
and can also discriminate strains carrying antibiotic resistance  
single-nucleotide polymorphism mutations. Finally, the assay is similarly  
capable of discriminating between bacterial species through  
reporter-specific discrimination and allele-specific amplification.  
Anchored **strand** displacement amplification allows multiplex  
amplification and complex genotype discrimination on the same platform.  
This assay simplifies the bacterial identification process greatly,  
allowing mol. biol. techniques to be performed with minimal processing of  
samples and practical experience.  
REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L99 ANSWER 2 OF 42 CAPLUS COPYRIGHT 2002 ACS  
ACCESSION NUMBER: 2002:595044 CAPLUS  
DOCUMENT NUMBER: 137:151084  
TITLE: Fluorescence polarization for analysis of DNA cytosine  
methylation  
INVENTOR(S): Berlin, Kurt  
PATENT ASSIGNEE(S): Epigenomics A.-G., Germany  
SOURCE: PCT Int. Appl., 30 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002061123	A2	20020808	WO 2002-EP922	20020129
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ,			

L72 2504 SEA FILE=BIOTECHDS ABB=ON (MICROARRAY# OR BIOCHIP# OR BIO  
CHIP# OR MICRO(A)ARRAY#)  
L74 278 SEA FILE=BIOTECHDS ABB=ON BUNDL?  
L75 3744 SEA FILE=BIOTECHDS ABB=ON STRAND#  
L77 205 SEA FILE=BIOTECHDS ABB=ON AXES  
L83 0 SEA FILE=BIOTECHDS ABB=ON L72 AND (L74 OR L75) AND L77

=> d que 185; d que 189; s (185 or 189)

L72 2504 SEA FILE=BIOTECHDS ABB=ON (MICROARRAY# OR BIOCHIP# OR BIO  
CHIP# OR MICRO(A)ARRAY#)  
L78 1765 SEA FILE=BIOTECHDS ABB=ON DATABA? OR DATA BA###  
L79 18644 SEA FILE=BIOTECHDS ABB=ON MICROB?(2A)INHIBIT? OR ANTIBIOTIC?  
OR ANTIMICROB? OR ANTI(W)(BIOTIC? OR MICROB?) OR MICROBICID?  
OR BACTERICID? OR BACTERIOSTAT?  
L85 1 SEA FILE=BIOTECHDS ABB=ON L72 AND L78 AND L79

L72 2504 SEA FILE=BIOTECHDS ABB=ON (MICROARRAY# OR BIOCHIP# OR BIO  
CHIP# OR MICRO(A)ARRAY#)  
L74 278 SEA FILE=BIOTECHDS ABB=ON BUNDL?  
L75 3744 SEA FILE=BIOTECHDS ABB=ON STRAND#  
L86 7732 SEA FILE=BIOTECHDS ABB=ON DRUG SCREENING/CT  
L87 817 SEA FILE=BIOTECHDS ABB=ON DATABASE/CT  
L89 11 SEA FILE=BIOTECHDS ABB=ON L72 AND L87 AND L86 AND (L74 OR  
L75)

L98 12 (L85 OR L89)

=> dup rem 194,196,197,198,195

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FILE 'WPIDS' ENTERED AT 11:02:36 ON 13 NOV 2002  
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PROCESSING COMPLETED FOR L94  
PROCESSING COMPLETED FOR L96  
PROCESSING COMPLETED FOR L97  
PROCESSING COMPLETED FOR L98  
PROCESSING COMPLETED FOR L95

L99 42 DUP REM L94 L96 L97 L98 L95 (4 DUPLICATES REMOVED)  
ANSWERS '1-10' FROM FILE CAPLUS  
ANSWERS '11-17' FROM FILE BIOSIS  
ANSWERS '18-21' FROM FILE BIOTECHNO  
ANSWERS '22-33' FROM FILE BIOTECHDS  
ANSWERS '34-42' FROM FILE WPIDS

=> d ibib ab 1-42; fil hom

L58 3419 SEA FILE=BIOTECHNO ABB=ON (MICROARRAY# OR BIOCHIP# OR BIO  
CHIP# OR MICRO(A)ARRAY#)  
L61 45 SEA FILE=BIOTECHNO ABB=ON CARTESIAN?  
L66 2 SEA FILE=BIOTECHNO ABB=ON L58 AND L61

L58 3419 SEA FILE=BIOTECHNO ABB=ON (MICROARRAY# OR BIOCHIP# OR BIO  
CHIP# OR MICRO(A)ARRAY#)  
L59 3131 SEA FILE=BIOTECHNO ABB=ON BUNDL?  
L60 25992 SEA FILE=BIOTECHNO ABB=ON STRAND#  
L62 1060 SEA FILE=BIOTECHNO ABB=ON AXES  
L63 9732 SEA FILE=BIOTECHNO ABB=ON DATABA?  
L64 35168 SEA FILE=BIOTECHNO ABB=ON MICROB?(2A)INHIBIT? OR ANTIBIOTIC?  
OR ANTIMICROB? OR ANTI(W) (BIOTIC? OR MICROB?) OR MICROBICID?  
OR BACTERICID? OR BACTEROSTAT?  
L68 3 SEA FILE=BIOTECHNO ABB=ON L58 AND (L59 OR L60) AND (L62 OR  
L63 OR L64)

L58 3419 SEA FILE=BIOTECHNO ABB=ON (MICROARRAY# OR BIOCHIP# OR BIO  
CHIP# OR MICRO(A)ARRAY#)  
L63 9732 SEA FILE=BIOTECHNO ABB=ON DATABA?  
L64 35168 SEA FILE=BIOTECHNO ABB=ON MICROB?(2A)INHIBIT? OR ANTIBIOTIC?  
OR ANTIMICROB? OR ANTI(W) (BIOTIC? OR MICROB?) OR MICROBICID?  
OR BACTERICID? OR BACTEROSTAT?  
L69 3 SEA FILE=BIOTECHNO ABB=ON L58 AND L63 AND L64

=> s (l66 or l68 or l69) not l65

L97 8 (L66 OR L68 OR L69) NOT L65 *previously printed*

=> fil biotechds

FILE 'BIOTECHDS' ENTERED AT 11:02:01 ON 13 NOV 2002  
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FILE LAST UPDATED: 7 NOV 2002 <20021107/UP>

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>>> NEW CLASSIFICATION SYSTEM FROM 2002 ONWARDS - SEE HELP CLA <<<

=> d que 180; d que 181; d que 183

L72 2504 SEA FILE=BIOTECHDS ABB=ON (MICROARRAY# OR BIOCHIP# OR BIO  
CHIP# OR MICRO(A)ARRAY#)  
L74 278 SEA FILE=BIOTECHDS ABB=ON BUNDL?  
L75 3744 SEA FILE=BIOTECHDS ABB=ON STRAND#  
L80 0 SEA FILE=BIOTECHDS ABB=ON L72 AND L74 AND L75

L72 2504 SEA FILE=BIOTECHDS ABB=ON (MICROARRAY# OR BIOCHIP# OR BIO  
CHIP# OR MICRO(A)ARRAY#)  
L76 5 SEA FILE=BIOTECHDS ABB=ON CARTESIAN?  
L81 0 SEA FILE=BIOTECHDS ABB=ON L72 AND L76

L95 9 (L24 OR L30 OR L33 OR L38) NOT (L21) *previously printed*  
=> fil biosis

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FILE COVERS 1969 TO DATE.  
CAS REGISTRY NUMBERS AND CHEMICAL NAMES (CNs) PRESENT  
FROM JANUARY 1969 TO DATE.

RECORDS LAST ADDED: 7 November 2002 (20021107/ED)

=> d que 152; d que 153; d que 154

L42 5240 SEA FILE=BIOSIS ABB=ON (MICROARRAY# OR BIOCHIP# OR BIO CHIP#  
OR MICRO(A)ARRAY#)  
L44 32439 SEA FILE=BIOSIS ABB=ON BUNDL?  
L45 74990 SEA FILE=BIOSIS ABB=ON STRAND?  
L47 9102 SEA FILE=BIOSIS ABB=ON AXES  
L48 30116 SEA FILE=BIOSIS ABB=ON DATABA?  
L49 176471 SEA FILE=BIOSIS ABB=ON MICROB?(2A)INHIBIT? OR ANTIBIOTIC? OR  
ANTIMICROB? OR ANTI(W)(BIOTIC? OR MICROB?) OR MICROBICID? OR  
BACTERICID? OR BACTEROSTAT?  
L52 2 SEA FILE=BIOSIS ABB=ON L42 AND (L44 OR L45) AND (L47 OR L48  
OR L49)

L42 5240 SEA FILE=BIOSIS ABB=ON (MICROARRAY# OR BIOCHIP# OR BIO CHIP#  
OR MICRO(A)ARRAY#)  
L46 621 SEA FILE=BIOSIS ABB=ON CARTESIAN?  
L53 3 SEA FILE=BIOSIS ABB=ON L42 AND L46

L42 5240 SEA FILE=BIOSIS ABB=ON (MICROARRAY# OR BIOCHIP# OR BIO CHIP#  
OR MICRO(A)ARRAY#)  
L48 30116 SEA FILE=BIOSIS ABB=ON DATABA?  
L49 176471 SEA FILE=BIOSIS ABB=ON MICROB?(2A)INHIBIT? OR ANTIBIOTIC? OR  
ANTIMICROB? OR ANTI(W)(BIOTIC? OR MICROB?) OR MICROBICID? OR  
BACTERICID? OR BACTEROSTAT?  
L54 2 SEA FILE=BIOSIS ABB=ON L42 AND L48 AND L49

=> s (152 or 153 or 154) not 143

L96 7 (L52 OR L53 OR L54) NOT (L43) *previously printed*  
=> fil biotechno

FILE 'BIOTECHNO' ENTERED AT 11:01:58 ON 13 NOV 2002  
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FILE LAST UPDATED: 7 NOV 2002 <20021107/UP>  
FILE COVERS 1980 TO DATE.

>>> SIMULTANEOUS LEFT AND RIGHT TRUNCATION AVAILABLE IN  
/CT AND BASIC INDEX <<<

=> d que 166; d que 168; d que 169

=> fil wpids

FILE 'WPIDS' ENTERED AT 11:01:50 ON 13 NOV 2002  
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FILE LAST UPDATED: 8 NOV 2002 <20021108/UP>  
MOST RECENT DERWENT UPDATE: 200272 <200272/DW>  
DERWENT WORLD PATENTS INDEX\*SUBSCRIBER FILE, COVERS 1963 TO DATE

>>> PATENT IMAGES AVAILABLE FOR PRINT AND DISPLAY >>>

>>> FOR DETAILS OF THE PATENTS COVERED IN CURRENT UPDATES,  
SEE <http://www.derwent.com/dwpi/updates/dwpicov/index.html> <<<

>>> FOR A COPY OF THE DERWENT WORLD PATENTS INDEX STN USER GUIDE,  
PLEASE VISIT:  
[http://www.stn-international.de/training\\_center/patents/stn\\_guide.pdf](http://www.stn-international.de/training_center/patents/stn_guide.pdf) <<<

>>> FOR INFORMATION ON ALL DERWENT WORLD PATENTS INDEX USER  
GUIDES, PLEASE VISIT:  
[http://www.derwent.com/userguides/dwpi\\_guide.html](http://www.derwent.com/userguides/dwpi_guide.html) <<<

=> d que 124; d que 130; d que 133;d que 138

L22 2373 SEA FILE=WPIDS ABB=ON (MICROARRAY# OR BIOCHIP# OR BIO CHIP#  
OR MICRO(A)ARRAY#)  
L23 1254 SEA FILE=WPIDS ABB=ON CARTESIAN?  
L24 1 SEA FILE=WPIDS ABB=ON L22 AND L23

L22 2373 SEA FILE=WPIDS ABB=ON (MICROARRAY# OR BIOCHIP# OR BIO CHIP#  
OR MICRO(A)ARRAY#)  
L25 62061 SEA FILE=WPIDS ABB=ON DATABA? OR DATA BA###  
L26 52778 SEA FILE=WPIDS ABB=ON MICROB?(2A)INHIBIT? OR ANTIBIOTIC? OR  
ANTIMICROB? OR ANTI(W)(BIOTIC? OR MICROB?) OR MICROBICID? OR  
BACTERICID? OR BACTEROSTAT?  
L30 1 SEA FILE=WPIDS ABB=ON L22 AND L25 AND L26

L22 2373 SEA FILE=WPIDS ABB=ON (MICROARRAY# OR BIOCHIP# OR BIO CHIP#  
OR MICRO(A)ARRAY#)  
L25 62061 SEA FILE=WPIDS ABB=ON DATABA? OR DATA BA###  
L26 52778 SEA FILE=WPIDS ABB=ON MICROB?(2A)INHIBIT? OR ANTIBIOTIC? OR  
ANTIMICROB? OR ANTI(W)(BIOTIC? OR MICROB?) OR MICROBICID? OR  
BACTERICID? OR BACTEROSTAT?  
L27 36669 SEA FILE=WPIDS ABB=ON BUNDL?  
L28 34529 SEA FILE=WPIDS ABB=ON STRAND#  
L33 4 SEA FILE=WPIDS ABB=ON L22 AND (L27 OR L28) AND (L25 OR L26)

L22 2373 SEA FILE=WPIDS ABB=ON (MICROARRAY# OR BIOCHIP# OR BIO CHIP#  
OR MICRO(A)ARRAY#)  
L29 85896 SEA FILE=WPIDS ABB=ON AXES  
L35 9 SEA FILE=WPIDS ABB=ON L22 AND L29  
L37 4 SEA FILE=WPIDS ABB=ON L35 AND D/DC  
L38 3 SEA FILE=WPIDS ABB=ON L37 NOT ROTORS/TI

=> s (124 or 130 or 133 or 138) not 121



=> fil capl

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*text  
search*

FILE COVERS 1907 - 13 Nov 2002 VOL 137 ISS 20  
FILE LAST UPDATED: 12 Nov 2002 (20021112/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

CAS roles have been modified effective December 16, 2001. Please check your SDI profiles to see if they need to be revised. For information on CAS roles, enter HELP ROLES at an arrow prompt or use the CAS Roles thesaurus (/RL field) in this file.

=> d que l6;d que l15; d que l16

L4 8481 SEA FILE=CAPLUS ABB=ON (MICROARRAY# OR BIOCHIP# OR BIO CHIP#  
OR MICRO(A)ARRAY#)/OBI  
L5 2710 SEA FILE=CAPLUS ABB=ON CARTESIAN?  
L6 1 SEA FILE=CAPLUS ABB=ON L4 AND L5 "

L4 8481 SEA FILE=CAPLUS ABB=ON (MICROARRAY# OR BIOCHIP# OR BIO CHIP#  
OR MICRO(A)ARRAY#)/OBI  
L7 32286 SEA FILE=CAPLUS ABB=ON BUNDL?  
L8 62357 SEA FILE=CAPLUS ABB=ON STRAND#  
L9 35192 SEA FILE=CAPLUS ABB=ON DATABA?  
L10 656 SEA FILE=CAPLUS ABB=ON MICROBIAL INHIBIT?  
L11 30645 SEA FILE=CAPLUS ABB=ON ANTIMICROB?/OBI  
L12 99969 SEA FILE=CAPLUS ABB=ON ANTIBIOTIC#/OBI  
L13 184 SEA FILE=CAPLUS ABB=ON L4 AND (L7 OR L8)  
L15 8 SEA FILE=CAPLUS ABB=ON L13 AND (L9 OR L10 OR L11 OR L12)

L4 8481 SEA FILE=CAPLUS ABB=ON (MICROARRAY# OR BIOCHIP# OR BIO CHIP#  
OR MICRO(A)ARRAY#)/OBI  
L9 35192 SEA FILE=CAPLUS ABB=ON DATABA?  
L10 656 SEA FILE=CAPLUS ABB=ON MICROBIAL INHIBIT?  
L11 30645 SEA FILE=CAPLUS ABB=ON ANTIMICROB?/OBI  
L12 99969 SEA FILE=CAPLUS ABB=ON ANTIBIOTIC#/OBI  
L16 1 SEA FILE=CAPLUS ABB=ON L4 AND L9 AND (L10 OR L11 OR L12)

=> s (l6 or l15 or l16) not l3

L94 10 (L6 OR L15 OR L16) NOT (L3) *previously printed w/ inventor search*

formation by prior art methods. Interrogation of the array means the noting of some specific different change in individual members, for purposes of qualitative or quantitative investigation. These changes may be any of the following; visual inspection, chemical deposition, electrical probing, mechanical or magnetic sensing, and capacitance change. The arrays can be used in this way for rapid screening in a wide variety of technological fields, including chemistry, genetics, immunology, material sciences, medicine (pharmaceuticals), molecular biology, and pharmacology. Examples of substance samples which can be investigated as an array include zinc, sulfur, gold, and metallic alloys, or polynucleotides, DNA and RNA or their fragments, both sense and antisense, peptides, proteins, glycoproteins, lipoproteins, carbohydrates, lipids, immunoglobulins, viruses, chromosomes, mitochondria, prokaryotic or eukaryotic cells, archaebacteria, ceramics, glasses, semiconductors or superconductors, plastics or other polymeric materials, woods, fabrics, and concretes. Of special interest are high density arrays of nucleic acids, which can be applied to ascertaining gene sequences, and detecting genetic mutations qualitative or quantitative differential expression of gene products; peptides, for mapping epitopic sequences which elicit immune responses; and screening for an activity in an array for development of pharmaceutical agents; and the traditional use for synthesising a large number of target substances in situ.

ADVANTAGE - The method is more rapid than prior art array assembly; typically individual application of target substances to a support, or synthesising them at specific locations on the support. The prior art method can also only produce a limited number of identical arrays at one time.

1,2,3/16

WO 9913313	A1		WO 1998-US10243	19980519
AU 9874985	A		AU 1998-74985	19980519
EP 1012564	A1		EP 1998-922436	19980519
CN 1269883	A		WO 1998-US10243	19980519
AU 733589	B		CN 1998-809024	19980519
AU 2001043856	A	Div ex	AU 1998-74985	19980519
AU 2001043857	A	Div ex	AU 2001-43856	20010511
AU 2001043858	A	Div ex	AU 1998-74985	19980519
US 2001019827	A1	Div ex Cont of	AU 2001-43857	20010511
JP 2001515735	W		AU 1998-74985	19980519
EP 1176413	A2	Div ex	AU 2001-43858	20010511
AU 743176	B	Div ex	US 1997-927974	19970911
AU 743220	B	Div ex	US 1998-145140	19980828
AU 744815	B	Div ex	US 2001-827505	20010406
EP 1207383	A2	Div ex	WO 1998-US10243	19980519
			JP 2000-511049	19980519
			EP 1998-922436	19980519
			EP 2001-203717	19980519
			AU 1998-74985	19980519
			AU 2001-43857	20010511
			AU 1998-74985	19980519
			AU 2001-43856	20010511
			AU 1998-74985	19980519
			AU 2001-43858	20010511
			EP 1998-922436	19980519
			EP 2001-203716	19980519

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 9874985	A	Based on	WO 9913313
EP 1012564	A1	Based on	WO 9913313
AU 733589	B	Previous Publ.	AU 9874985
		Based on	WO 9913313
AU 2001043856	A	Div ex	AU 733589
AU 2001043857	A	Div ex	AU 733589
AU 2001043858	A	Div ex	AU 733589
JP 2001515735	W	Based on	WO 9913313
EP 1176413	A2	Div ex	EP 1012564
AU 743176	B	Previous Publ.	AU 200143857
		Div ex	AU 733589
AU 743220	B	Previous Publ.	AU 200143856
		Div ex	AU 733589
AU 744815	B	Previous Publ.	AU 200143858
		Div ex	AU 733589
EP 1207383	A2	Div ex	EP 1012564

PRIORITY APPLN. INFO: US 1997-927974 19970911; AU 2001-43856  
 20010511; AU 2001-43857 20010511; AU  
 2001-43858 20010511; US 1998-145140  
 19980828; US 2001-827505 20010406

AB WO 9913313 A UPAB: 20011001

NOVELTY - Production of high density target substance arrays, by sectioning a bundle of target strands comprising the target substances; and including also the optional steps of:

- (1) stabilizing the bundle;
- (2) incorporating additional material into the bundle; and
- (3) interrogating the array.

USE - The method produces large numbers of identical arrays rapidly, simultaneously, and cost effectively, and is able to use a wide variety of target substances and supports, including some not amenable to array

DOCUMENT NUMBER: PREV199800068789  
TITLE: Use of a 10,000 gene cDNA **microarray** to analyze gene expression patterns in hematological disorders.  
AUTHOR(S): Ross, D. T. (1); Eisen, M.; Lashkari, D.; Shuler, G.; Boguski, M.; **Hudson, J.**; Botstein, D.; Shalon, D.; Brown, P. O. (1)  
CORPORATE SOURCE: (1) Dep. Biochem., Howard Hughes Med. Inst., Stanford Univ., Stanford, CA USA  
SOURCE: Blood, (Nov. 15, 1997) Vol. 90, No. 10 SUPPL. 1 PART 1, pp. 557A.  
Meeting Info.: 39th Annual Meeting of the American Society of Hematology San Diego, California, USA December 5-9, 1997  
The American Society of Hematology  
. ISSN: 0006-4971.  
DOCUMENT TYPE: Conference  
LANGUAGE: English

L93 ANSWER 14 OF 14 WPIDS (C) 2002 THOMSON DERWENT  
ACCESSION NUMBER: 1999-254284 [21] WPIDS  
DOC. NO. NON-CPI: N1999-189331  
DOC. NO. CPI: C1999-074316  
TITLE: Production of high density target substance arrays.  
DERWENT CLASS: A96 B04 B07 D16 J04 S03  
INVENTOR(S): **DAWSON, E P; HUDSON, J R**  
PATENT ASSIGNEE(S): (BIOV-N) BIOVENTURES INC; (GENO-N) GENOVATIONS INC;  
(DAWS-I) DAWSON E P; (HUDS-I) HUDSON J R  
COUNTRY COUNT: 82  
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9913313	A1	19990318	(199921)*	EN	5
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG ZW					
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE GH HU ID IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZW					
AU 9874985	A	19990329	(199932)		
EP 1012564	A1	20000628	(200035)	EN	
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI					
CN 1269883	A	20001011	(200103)		
AU 733589	B	20010517	(200134)		
AU 2001043856	A	20010802	(200152)#		
AU 2001043857	A	20010802	(200152)#		
AU 2001043858	A	20010802	(200152)#		
US 2001019827	A1	20010906	(200154)		
JP 2001515735	W	20010925	(200170)		47
EP 1176413	A2	20020130	(200216)	EN	
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI					
AU 743176	B	20020117	(200219)#		
AU 743220	B	20020124	(200221)#		
AU 744815	B	20020307	(200229)#		
EP 1207383	A2	20020522	(200241)	EN	
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI					

## APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
-----------	------	-------------	------

Boguski, Mark S.; Lashkari, Deval; Shalon, Dari; Botstein, David; Brown, Patrick O. (1)  
CORPORATE SOURCE: (1) Dep. Biochem., Howard Hughes Med. Inst., Stanford Univ. Sch. Med., Stanford, CA 94305 USA  
SOURCE: Science (Washington D C), (Jan. 1, 1999) Vol. 283, No. 5398, pp. 83-87.  
ISSN: 0036-8075.

DOCUMENT TYPE: Article

LANGUAGE: English

AB The temporal program of gene expression during a model physiological response of human cells, the response of fibroblasts to serum, was explored with a complementary DNA **microarray** representing about 8600 different human genes. Genes could be clustered into groups on the basis of their temporal patterns of expression in this program. Many features of the transcriptional program appeared to be related to the physiology of wound repair, suggesting that fibroblasts play a larger and richer role in this complex multicellular response than had previously been appreciated.

L93 ANSWER 11 OF 14 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

ACCESSION NUMBER: 1998:196955 BIOSIS

DOCUMENT NUMBER: PREV199800196955

TITLE: Gene expression analysis of prostate cancer progression by laser capture microdissection and high density cDNA **microarrays**.

AUTHOR(S): Krizman, D. (1); Emmert-Buck, M.; Elkahloun, A.; Becker, K.; Chuaqui, R.; Kole, K.; Bittner, M.; Chen, Y.; Linehan, W.; Hudson, J.; Liotta, L.; Meltzer, P.; Trent, J.

CORPORATE SOURCE: (1) Natl. Cancer Inst., Natl. Human Genome Res. Inst., Bethesda, MD 20892 USA

SOURCE: Proceedings of the American Association for Cancer Research Annual Meeting, (March, 1998) Vol. 39, pp. 453.  
Meeting Info.: 89th Annual Meeting of the American Association for Cancer Research New Orleans, Louisiana, USA March 28-April 1, 1998 American Association for Cancer Research  
. ISSN: 0197-016X.

DOCUMENT TYPE: Conference

LANGUAGE: English

L93 ANSWER 12 OF 14 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

ACCESSION NUMBER: 1997:420835 BIOSIS

DOCUMENT NUMBER: PREV199799720038

TITLE: Use of DNA **microarrays** to monitor differential gene expression in yeast and humans.

AUTHOR(S): Iyer, Vishwanath (1); Derisi, Joseph (1); Eisen, Michael; Ross, Douglas (1); Spellman, Paul; Hudson, James, Jr.; Schuler, Greg; Lashkari, Deval; Shalon, Dari; Botstein, David; Brown, Patrick (1)

CORPORATE SOURCE: (1) Dep. Biochem., Stanford Univ., Stanford, CA USA

SOURCE: FASEB Journal, (1997) Vol. 11, No. 9, pp. A1126.  
Meeting Info.: 17th International Congress of Biochemistry and Molecular Biology in conjunction with the Annual Meeting of the American Society for Biochemistry and Molecular Biology San Francisco, California, USA August 24-29, 1997  
ISSN: 0892-6638.

DOCUMENT TYPE: Conference; Abstract

LANGUAGE: English

L93 ANSWER 13 OF 14 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

ACCESSION NUMBER: 1998:68789 BIOSIS

SOURCE: Laboratory Investigation, (March, 2000) Vol. 80, No. 3, pp. 144A. print.  
Meeting Info.: Annual Meeting of the United States and Canadian Academy of Pathology New Orleans, Louisiana, USA March 25-31, 2000  
ISSN: 0023-6837.

DOCUMENT TYPE: Conference  
LANGUAGE: English  
SUMMARY LANGUAGE: English

L93 ANSWER 8 OF 14 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

ACCESSION NUMBER: 2000:171497 BIOSIS

DOCUMENT NUMBER: PREV200000171497

TITLE: Gene expression in large B-cell lymphoma: cDNA **microarray** analysis.

AUTHOR(S): Chan, W. C. (1); Alizadeh, A.; Eisen, M.; Davis, R. E.; Ma, C.; Sabet, H.; Tran, T.; Powell, J. I.; Yang, L.; Greiner, T. C. (1); Weisenburger, D. D. (1); Armitage, J. O. (1); Marti, G. E.; Moores, T.; **Hudson**, J.; Lossos, I.; Warnke, R.; Levy, R.; Botstein, D.; Brown, P. O.; Staudt, L. M.

CORPORATE SOURCE: (1) University of Nebraska Medical Center, Omaha, NB USA  
SOURCE: Laboratory Investigation., (Jan., 2000) Vol. 80, No. 1, pp. 144A.  
Meeting Info.: 2000 Annual Meeting United States and Canadian Academy of Pathology. New Orleans, Louisiana, USA March 25-31, 2000  
ISSN: 0023-6837.

DOCUMENT TYPE: Conference  
LANGUAGE: English  
SUMMARY LANGUAGE: English

L93 ANSWER 9 OF 14 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

ACCESSION NUMBER: 2000:44439 BIOSIS

DOCUMENT NUMBER: PREV200000044439

TITLE: Gene expression in large B-cell lymphoma using cDNA **microarray** technology.

AUTHOR(S): Chan, W. C. (1); Alizadeh, A.; Eisen, M.; Davis, R. E.; Ma, C.; Sabet, H.; Tran, T.; Powell, J. I.; Yang, L.; Greiner, T. C. (1); Weisenburger, D. D. (1); Armitage, J. O. (1); Marti, G. E.; Moores, T.; **Hudson**, J.; Lossos, I.; Warnke, R.; Levy, R.; Botstein, D.; Brown, P. O.; Staudt, L. M.

CORPORATE SOURCE: (1) Departments of Pathology and Microbiology, and Medicine, University of Nebraska Medical Center, Omaha, NE USA

SOURCE: Blood, (Nov. 15, 1999) Vol. 94, No. 10 SUPPL. 1 PART 1, pp. 698a.  
Meeting Info.: Forty-first Annual Meeting of the American Society of Hematology New Orleans, Louisiana, USA December 3-7, 1999 The American Society of Hematology  
. ISSN: 0006-4971.

DOCUMENT TYPE: Conference  
LANGUAGE: English

L93 ANSWER 10 OF 14 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

ACCESSION NUMBER: 1999:57907 BIOSIS

DOCUMENT NUMBER: PREV199900057907

TITLE: The transcriptional program in the response of human fibroblasts to serum.

AUTHOR(S): Iyer, Vishwanath R.; Eisen, Michael B.; Ross, Douglas T.; Schuler, Greg; Moore, Troy; Lee, Jeffrey C. F.; Trent, Jeffrey M.; Staudt, Louis M.; **Hudson**, James, Jr.;

that some HUCB-derived cells (recognized by anti-human nuclei labeling) were immunopositive for glial fibrillary acidic protein (GFAP) and few donor cells expressed the neuronal marker TuJ1 (class III beta-tubulin). These findings suggest that at least some of the transplanted HUCB cells differentiated into cells with distinct glial or neuronal phenotypes after being exposed to instructive signals from the developing brain.

L93 ANSWER 6 OF 14 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.  
ACCESSION NUMBER: 2000:266223 BIOSIS  
DOCUMENT NUMBER: PREV200000266223  
TITLE: Distinct types of diffuse large B-cell lymphoma identified by gene expression profiling.  
AUTHOR(S): Alizadeh, Ash A.; Eisen, Michael B.; Davis, R. Eric; Ma, Chi; Lossos, Izidore S.; Rosenwald, Andreas; Boldrick, Jennifer C.; Sabet, Hajeer; Tran, Truc; Yu, Xin; Powell, John I.; Yang, Liming; Marti, Gerald E.; Moore, Troy; **Hudson, James, Jr.**; Lu, Lisheng; Lewis, David B.; Tibshirani, Robert; Sherlock, Gavin; Chan, Wing C.; Greiner, Timothy C.; Weisenburger, Dennis D.; Armitage, James O.; Warnke, Roger; Levy, Ronald; Wilson, Wyndham; Grever, Michael R.; Byrd, John C.; Botstein, David; Brown, Patrick O. (1); Staudt, Louis M.  
CORPORATE SOURCE: (1) Department of Biochemistry, Stanford University School of Medicine, Stanford, CA, 94305 USA  
SOURCE: Nature (London), (Feb. 3, 2000) Vol. 403, No. 6769, pp. 503-511. print..  
ISSN: 0028-0836.  
DOCUMENT TYPE: Article  
LANGUAGE: English  
SUMMARY LANGUAGE: English

AB Diffuse large B-cell lymphoma (DLBCL), the most common subtype of non-Hodgkin's lymphoma, is clinically heterogeneous: 40% of patients respond well to current therapy and have prolonged survival, whereas the remainder succumb to the disease. We proposed that this variability in natural history reflects unrecognized molecular heterogeneity in the tumours. Using DNA **microarrays**, we have conducted a systematic characterization of gene expression in B-cell malignancies. Here we show that there is diversity in gene expression among the tumours of DLBCL patients, apparently reflecting the variation in tumour proliferation rate, host response and differentiation state of the tumour. We identified two molecularly distinct forms of DLBCL which had gene expression patterns indicative of different stages of B-cell differentiation. One type expressed genes characteristic of germinal centre B cells ('germinal centre B-like DLBCL'); the second type expressed genes normally induced during in vitro activation of peripheral blood B cells ('activated B-like DLBCL'). Patients with germinal centre-B like DLBCL had a significantly better overall survival than those with activated B-like DLBCL. The molecular classification of tumours on the basis of gene expression can thus identify previously undetected and clinically significant subtypes of cancer.

L93 ANSWER 7 OF 14 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.  
ACCESSION NUMBER: 2000:523731 BIOSIS  
DOCUMENT NUMBER: PREV200000523731  
TITLE: Gene expression in large B-cell lymphoma: cDNA **microarray** analysis.  
AUTHOR(S): Chan, W. C. (1); Alizadeh, A.; Eisen, M.; Davis, R. E.; Ma, C.; Sabet, H.; Tran, T.; Powell, J. I.; Yang, L.; Greiner, T. C. (1); Weisenburger, D. D. (1); Armitage, J. O. (1); Marti, G. E.; Moores, T.; **Hudson, J.**; Lossos, I.; Warnke, R.; Levy, R.; Botstein, D.; Brown, P. O.; Staudt, L. M.  
CORPORATE SOURCE: (1) University of Nebraska Medical Center, Omaha, NE USA

G. (1)  
CORPORATE SOURCE: (1) Microarrays Department, Research Genetics, Inc., 2700  
Memorial Parkway, Huntsville, AL USA  
SOURCE: Cancer Research, (Nov. 15, 1999) Vol. 59, No. 22, pp.  
5656-5661.  
ISSN: 0008-5472.  
DOCUMENT TYPE: Article  
LANGUAGE: English  
SUMMARY LANGUAGE: English  
AB The development and use of molecular-based therapy for breast cancer and  
other human malignancies will require a detailed molecular genetic  
analysis of patient tissues. The recent development of laser capture  
microdissection and high density cDNA arrays now provides a unique  
opportunity to generate gene expression profiles of cells from various  
stages of tumor progression as it occurs in the actual neoplastic tissue  
milieu. We report the combined use of laser capture microdissection and  
high-throughput cDNA **microarrays** to monitor in vivo gene  
expression levels in purified normal, invasive, and metastatic breast cell  
populations from a single patient. These in vivo gene expression profiles  
were verified by real-time quantitative PCR and immunohistochemistry. The  
combined use of laser capture microdissection and cDNA **microarray**  
analysis provides a powerful new approach to elucidate the in vivo  
molecular events surrounding the development and progression of breast  
cancer and is generally applicable to the study of malignancy.

L93 ANSWER 5 OF 14 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.  
ACCESSION NUMBER: 2002:383368 BIOSIS  
DOCUMENT NUMBER: PREV200200383368  
TITLE: Human umbilical cord blood cells express neural antigens  
after transplantation into the developing rat brain.  
AUTHOR(S): Zigova, Tanja (1); Song, Shijie; Willing, Alison E.;  
**Hudson, Jennifer E.**; Newman, Mary B.; Saporta,  
Samuel; Sanchez-Ramos, Juan; Sanberg, Paul R.  
CORPORATE SOURCE: (1) Department of Neurosurgery, College of Medicine,  
University of South Florida, 12901 B.B. Downs Blvd., Tampa,  
FL, 33612: tzigova@hsc.usf.edu USA  
SOURCE: Cell Transplantation, (2002) Vol. 11, No. 3, pp. 265-274.  
print.  
ISSN: 0963-6897.  
DOCUMENT TYPE: Article  
LANGUAGE: English  
AB Recently, our laboratory began to characterize the mononuclear cells from  
human umbilical cord blood (HUCB) both in vitro and in vivo. These  
cryopreserved human cells are available in unlimited quantities and it is  
believed that they may represent a source of cells with possible  
therapeutic and practical value. Our previous molecular and  
immunocytochemical studies on cultured HUCB cells revealed their ability  
to respond to nerve growth factor (NGF) by increased expression of neural  
markers typical for nervous system-derived stem cells. In addition, the  
DNA **microarray** detected downregulation of several genes  
associated with development of blood cell lines. To further explore the  
survival and phenotypic properties of HUCB cells we transplanted them into  
the developing rat brain, which is known to provide a conducive  
environment for development of neural phenotypes. Prior to  
transplantation, HUCB cells were either cultured with DMEM and fetal  
bovine serum or were exposed to retinoic acid (RA) and nerve growth factor  
(NGF). Neonatal pups (1 day old) received unilateral injection of cell  
suspension into the anterior part of subventricular zone. One month after  
transplantation animals were perfused, their brains cryosectioned, and  
immunocytochemistry was performed for identification of neural phenotypes.  
Our results clearly demonstrated that approximately 20% of transplanted  
HUCB survived (without immunosuppression) within the neonatal brain.  
Additionally, double-labeling with cell-type-specific markers revealed



cerevisiae have been synthesized by PCR using a set of .apprx.6000 primer pairs. Each of the forward primers has a common 22-base sequence at its 5' end, and each of the back primers has a common 20-base sequence at its 5' end. These common termini allow reamplification of the entire set of original PCR products using a single pair of longer primers-in our case, 70 bases. The resulting 70-base elements that flank each ORF can be used for rapid and efficient cloning into a linearized yeast vector that contains these same elements at its termini. This cloning by genetic recombination obviates the need for ligations or bacterial manipulations and should permit convenient global approaches to gene function that require the assay of each putative yeast gene.

L93 ANSWER 3 OF 14 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE  
1

ACCESSION NUMBER: 2000:229637 BIOSIS  
DOCUMENT NUMBER: PREV200000229637  
TITLE: Development of a prostate cDNA **microarray** and statistical gene expression analysis package.  
AUTHOR(S): Carlisle, Alex J.; Prabhu, Vinay V.; Elkahoul, Abdel; **Hudson, James**; Trent, Jeffrey M.; Linehan, W. Marston; Williams, Elizabeth D.; Emmert-Buck, Michael R.; Liotta, Lance A.; Munson, Peter J.; Krizman, David B. (1)  
CORPORATE SOURCE: (1) Advanced Technology Center-134F, 8717 Grovemont Circle, Gaithersburg, MD, 20877 USA  
SOURCE: Molecular Carcinogenesis, (May, 2000) Vol. 28, No. 1, pp. 12-22.  
ISSN: 0899-1987.  
DOCUMENT TYPE: Article  
LANGUAGE: English  
SUMMARY LANGUAGE: English

AB A cDNA **microarray** comprising 5184 different cDNAs spotted onto nylon membrane filters was developed for prostate gene expression studies. The clones used for arraying were identified by cluster analysis of > 35000 prostate cDNA library-derived expressed sequence tags (ESTs) present in the dbEST database maintained by the National Center for Biotechnology Information. Total RNA from two cell lines, prostate line 8.4 and melanoma line UACC903, was used to make radiolabeled probe for filter hybridizations. The absolute intensity of each individual cDNA spot was determined by phosphorimager scanning and evaluated by a bioinformatics package developed specifically for analysis of cDNA **microarray** experimentation. Results indicated 89% of the genes showed intensity levels above background in prostate cells compared with only 28% in melanoma cells. Replicate probe preparations yielded results with correlation values ranging from  $r=0.90$  to  $0.93$  and coefficient of variation ranging from 16 to 28%. Findings indicate that among others, the keratin 5 and vimentin genes were differentially expressed between these two divergent cell lines. Follow-up northern blot analysis verified these two expression changes, thereby demonstrating the reliability of this system. We report the development of a cDNA **microarray** system that is sensitive and reliable, demonstrates a low degree of variability, and is capable of determining verifiable gene expression differences between two distinct human cell lines. This system will prove useful for differential gene expression analysis in prostate-derived cells and tissue.

L93 ANSWER 4 OF 14 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE  
2

ACCESSION NUMBER: 2000:69931 BIOSIS  
DOCUMENT NUMBER: PREV200000069931  
TITLE: In vivo gene expression profile analysis of human breast cancer progression.  
AUTHOR(S): Sgroi, Dennis C.; Teng, Sarena; Robinson, Greg; LeVangie, Rebecca; **Hudson, James R., Jr.**; Elkahoul, Abdel

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PROCESSING COMPLETED FOR L65

PROCESSING COMPLETED FOR L21

L93 14 DUP REM L3 L43 L65 L21 (2 DUPLICATES REMOVED)

ANSWERS '1-2' FROM FILE CAPLUS

ANSWERS '3-13' FROM FILE BIOSIS

ANSWER '14' FROM FILE WPIDS

=> d ibib ab 1-14

L93 ANSWER 1 OF 14 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2000:45458 CAPLUS

DOCUMENT NUMBER: 133:100148

TITLE: Membrane-based microarrays

AUTHOR(S): Dawson, Elliott P.; Hudson, James;  
Steward, John; Donnell, Philip A.; Chan, Wing W.;  
Taylor, Richard F.

CORPORATE SOURCE: Genovations, Inc., Huntsville, AL, USA

SOURCE: Proceedings of SPIE-The International Society for  
Optical Engineering (1999), 3857(Cheical Microsensors  
and Applications II), 31-37  
CODEN: PSISDG; ISSN: 0277-786X

PUBLISHER: SPIE-The International Society for Optical Engineering

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Microarrays represent a new approach to the rapid detection and  
identification of analytes. Studies to date have shown that the  
immobilization of receptor mols. (such as DNA, oligonucleotides,  
antibodies, enzymes and binding proteins) onto silicon and polymeric  
substrates can result in arrays able to detect hundreds of analytes in a  
single step. The formation of the receptor/analyte complex can, itself,  
lead to detection, or the complex can be interrogated through the use of  
fluorescent, chemiluminescent or radioactive probes and ligands.

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L93 ANSWER 2 OF 14 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1998:49196 CAPLUS

DOCUMENT NUMBER: 128:189015

TITLE: The complete set of predicted genes from Saccharomyces  
cerevisiae in a readily usable form

AUTHOR(S): Hudson, James R., Jr.; Dawson, Elliott  
P.; Rushing, Kimerly, L.; Jackson, Cynthia H.;  
Lockshon, Daniel; Conover, Diana; Lanciault,  
Christian; Harris, James R.; Simmons, Steven J.;  
Rothstein, Rodney; Fields, Stanley

CORPORATE SOURCE: Research Genetics Inc., Huntsville, AL, 35801, USA

SOURCE: Genome Research (1997), 7(12), 1169-1173

CODEN: GEREFS; ISSN: 1088-9051

PUBLISHER: Cold Spring Harbor Laboratory Press

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Nearly all of the open reading frames (ORFs) the yeast Saccharomyces

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L42 5240 SEA FILE=BIOSIS ABB=ON (MICROARRAY# OR BIOCHIP# OR BIO CHIP#  
OR MICRO(A)ARRAY#)  
L43 11 SEA FILE=BIOSIS ABB=ON (L39 OR L40) AND L42

=> fil biotechno; d que l65

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L56 158 SEA FILE=BIOTECHNO ABB=ON HUDSON J?/AU  
L58 3419 SEA FILE=BIOTECHNO ABB=ON (MICROARRAY# OR BIOCHIP# OR BIO  
CHIP# OR MICRO(A)ARRAY#)  
L65 2 SEA FILE=BIOTECHNO ABB=ON (L55 OR L56) AND L58

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L71 10 SEA FILE=BIOTECHDS ABB=ON HUDSON J?/AU  
L72 2504 SEA FILE=BIOTECHDS ABB=ON (MICROARRAY# OR BIOCHIP# OR BIO  
CHIP# OR MICRO(A)ARRAY#)  
L73 0 SEA FILE=BIOTECHDS ABB=ON (L70 OR L71) AND L72

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inventors

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FILE LAST UPDATED: 12 Nov 2002 (20021112/ED)

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L2 1077 SEA FILE=CAPLUS ABB=ON HUDSON J?/AU  
L3 2 SEA FILE=CAPLUS ABB=ON L1 AND L2

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L19 20 SEA FILE=WPIDS ABB=ON DAWSON E?/AU  
L20 158 SEA FILE=WPIDS ABB=ON HUDSON J?/AU  
L21 1 SEA FILE=WPIDS ABB=ON L19 AND L20

=> fil biosis; d que 143